Paid Circulation, 24,339

The New England Journal of Medicine

FORMERLY THE BOSTON MEDICAL AND SURGICAL JOURNAL—*Established 1828*

VOLUME 239 DECEMBER 16, 1948 NUMBER 25

Delays and Errors in the Diagnosis of Brain Tumor 945
Fredrick C. Redlich, Rembrandt H. Dunsmore and Eugene B. Brody

The Effect of Subacute Bacterial Endocarditis on the Course of the Underlying Heart Disease 951
Bernard Rapoport and Laurence B. Ellis

Generalized Bullous Eruption Following Testing for Sulfonamide Hypersensitivity . . 956
David A. Straus

Fertility Studies in the Human Male with Traumatic Injuries of the Spinal Cord and Cauda Equina 959
Herbert W. Horne, David P. Paull and Donald Munro

Obituary 982

Massachusetts Medical Society 983

Correspondence 983

Medical Progress: Thoracic Surgery . . . . 961 (Concluded)
J. Gordon Scannell

Case Records of the Massachusetts General Hospital 972

Editorials:

One World 980

Massachusetts Physicians Committee 981

Undergraduate Instruction in Allergy 981

Guide to Health Services 982

Books Received 983

Notices 983

Entered as second-class matter, November 16, 1932, at the post office at Boston, Massachusetts, under the Act of March 3, 1879.

Now Published by Saunders

A. M. A. INTERNS' MANUAL

This little book has been written expressly for the intern, but it could very aptly be titled "Physicians' Manual," because its usefulness is by no means limited to the intern. It contains valuable information on a great variety of subjects—information that cannot elsewhere be found in such concise and usable form—information that is useful to every doctor.

The clinical data alone are worth the price of the book. There is a section on common emergencies (gastric hemorrhage, shock, convulsion etc.) and there is much valuable guidance on poisoning, drugs, tests, diets etc. The MANUAL will fit easily into the doctor's bag or desk drawer.

A. M. A. Interns' Manual. By the various Bureaus and Councils of the American Medical Association. Compiled and edited in the office of the Council on Pharmacy and Chemistry. 201 pages, 4¼" x 7⅛". $2.25. *New*

W. B. Saunders COMPANY

WEST WASHINGTON SQUARE, PHILADELPHIA 5

Advertisement

From where I sit *by* Joe Marsh

How to Celebrate Your Wedding Anniversary

The "Dutch" Millers celebrated their Tin Wedding Anniversary Saturday. Everything had to be tin. Folks even ate off tin plates, and drank coffee out of tin cups.

When it was time to drink a toast to the "bride and groom," out came the final touch: cold beer in cans. And come the Millers' 15th anniversary (Glass) I expect we'll be toasting them with sparkling beer in *bottles!*

And I just couldn't help thinking that there was a real lesson for married folks in the way that Dutch and his missus have got along together—in their policy of live-and-let-live, with never a criticism of each other's differences in taste.

From where I sit, it's due to two things: Temperance—as that moderate preference for beer suggests, and Tolerance—for their own differences of opinion—and for the tastes of others, whether applied to beer, to politics, or how to celebrate an anniversary.

Joe Marsh

Copyright, 1948, United States Brewers Foundation

THOMAS W. REED COMPANY
Physician's and Hospital Supplies

INVALID EQUIPMENT

Wheel Chairs . . Hospital Beds . . Sun Lamps . . Infra-Red Lamps . . Fracture Beds . . Invalid Walkers . . Short Wave Apparatus . . Commodes . . Overbed and Bedside Tables.

RENTAL SERVICE

Monthly rental payments can be arranged.

SICK ROOM SUPPLIES

Crutches . . Scales . . Surgical Dressings and so forth

CORRECTIVE APPLIANCES

Corsets . . Trusses . . Belts. Expert fitting by male and female attendants at all times.

533 Commonwealth Ave., Kenmore Square
Boston, Massachusetts
Telephone KE 6-1945

TWO-WAY PROTECTION

Tablets FERROSATE (Kenmore)
(Ferrous Sulfate, gr. iv)

are coated twice to provide a doubly protected Ferrous Sulfate offering these therapeutic advantages:

1 **Inner coating prevents premature oxidation in vivo.**

2 **Outer coating increases palatability and aids in preventing tooth discoloration.**

Write Dept. N12 for professional sample.

Kenmore Pharmacy, Inc.
500 Commonwealth Ave.
Boston, Mass. U.S.A.

MEMORIAL CANCER CENTER

offers

Two-year Residencies in Anesthesiology to graduates from approved medical schools who have had at least one year of approved internship.

One-year Fellowships in Anesthesiology available to physicians who have completed at least one year of training in anesthesiology.

For further information write to
OLGA SCHWEIZER, M.D.
MEMORIAL HOSPITAL
444 East 68th Street, New York 21, N. Y.

The New England
Journal of Medicine

Copyright, 1948, by the Massachusetts Medical Society

Volume 239 DECEMBER 16, 1948 Number 25

DELAYS AND ERRORS IN THE DIAGNOSIS OF BRAIN TUMOR*

FREDRICK C. REDLICH, M.D.,† REMBRANDT H. DUNSMORE, M.D.,‡ AND EUGENE B. BRODY, M.D.§
NEW HAVEN, CONNECTICUT

MOST general practitioners, internists and neuropsychiatrists with a sufficiently large and varied practice sooner or later have the distressing experience of mistaking a brain tumor for a psychoneurosis or of unnecessarily delaying the correct diagnosis. As in other disorders involving behavior, the opinions of family and friends, as well as of other lay people in the community, often contribute to confuse the opinions of the physician, particularly of the general practitioner. Such considerations stimulated the present investigation of diagnostic errors made in 100 proved cases of brain tumor.

It is impossible to extract a bibliography on diagnostic errors from the vast literature on brain tumors because such a diagnostic consideration is inextricably involved with other viewpoints in books and papers dealing with the general subject of brain tumors. However, it might be stated that the literature on diagnostic errors may be grouped under three headings. The first comprises general statements by neurologists, neurosurgeons and psychiatrists based on prolonged experience in which the authors reflect on their knowledge and offer their advice and warnings. Some of these reflections are contained in the great classics on the subject by Cushing, Bailey and so forth, and others in papers of the editorial type. A second group consists of case reports: there is a wide discrepancy between the classic monographs and the repetitive and often single and not always spectacular case reports. Characteristic of this group is emphasis on differential diagnosis between various tumors and other conditions or fine differentiations between the tumors themselves. The third group consists of reports on technics (cerebrospinal-fluid examinations, electroencephalography, radiologic diagnosis and so forth) that help to establish or facilitate the diagnosis of brain tumors. A few papers dealing explicitly with the diagnostic errors in brain tumors are listed.

Horrax[1] differentiated symptomatologically typical tumors easily diagnosed on the basis of adequate history, physical examination and laboratory study, and atypical ones that should be studied with the particular lesion in mind. He believed that a tumor or something simulating a tumor can almost always be diagnosed provided the patient consents to thorough diagnostic study. McIntyre and McIntyre[2] stated that most errors in the diagnosis of brain tumor were due to lack of "brain tumor consciousness" in the mind of the examiner; failure to realize the importance of an adequate history and repeated neurologic examinations; and failure to realize that headache, vomiting and choked disk are *not* early signs of brain tumor.

Purves-Stewart,[3] who reviewed 115 cases of verified brain tumors, concluded that carelessness or insufficient observation, as well as a tendency to cling to the first conception of the case, was the most important factor in what he called available errors. The main problems in what he termed unavailable errors were too short a period of observation and scanty clinical symptoms. A large majority of the diagnostic errors in the series of Hastings[4] were made in the differential diagnosis of cerebral vascular disease and tumor. Bing[5] discussed intracranial tumors with minimal focal signs presenting difficulties in diagnosis. Many authors have stressed the importance of tumor consideration in patients exhibiting convulsive seizures after the age of thirty. The great value of such technical diagnostic aids as electroencephalographic and air studies is generally recognized, and yet, as Poppen and Peacher[6] point out, these are not invariably reliable and cannot replace diagnostic weapons available to all: an adequate history and neurologic examination.

The present study approaches the problem from the viewpoint of public health. It has seemed that the differential diagnosis that concerns the neurologist so greatly actually contributes little to knowledge of why the diagnosis of brain tumors is unduly delayed or missed. The problem is not one of mak-

*From the Department of Psychiatry and the Department of Surgery, Yale University School of Medicine.
†Associate professor of psychiatry, Yale University School of Medicine; psychiatrist-in-chief, Grace-New Haven Community Hospital.
‡Instructor, Yale University School of Medicine; James Hudson Brown Memorial Fellow.
§Instructor, Department of Psychiatry, Yale University School of Medicine; resident, Psychiatric Clinic, Grace-New Haven Community Hospital.

ing a differential pathological type of diagnosis but of establishing the presence of an intracranial tumor at a stage sufficiently early so that treatment may be effective. The following specific questions must be answered: Does the examination of histories of proved cases of brain tumor suggest *unnecessary delays* in correct diagnosis? If such delays and errors are found, why do they occur? Who errs and what are the reasons for the errors? What remedies may be suggested?

Method

A random sample of 100 brain tumors verified by operation or autopsy or both was chosen and classified according to type and localization. The following aspects of the cases were tabulated: first complaints; first neurologic signs detected; correct and false diagnosis by family physicians; correct and false diagnosis after hospitalization before diagnostic study by specialists; correct and false diagnosis by specialists (neurologists, psychiatrists and neurosurgeons); diagnostic contributions of cerebrospinal-fluid studies, air studies and radiologic and electroencephalographic examinations; and time lost between the first appearance of signs and symptoms (when the diagnosis presumably could have been made) and the time of the correct diagnosis.

More than one first complaint was often mentioned, but for purposes of tabulation these were broken down into single symptoms (Table 1). Thus, a certain amount of distortion and condensation was unavoidable.

Table 1. *First Complaints.*

Complaint	No. of Cases
Headaches	86
Disturbance of eyesight (amblyopia, amaurosis, blurred vision, scotoma and so forth)	36
Gastrointestinal symptoms:	
Vomiting	32
Nausea without vomiting	27
Seizures	30
Locomotor unsteadiness (falling, lack of co-ordination and so forth)	29
Double vision, ptosis and so forth	21
Weakness of limbs	21
Personality changes (neurotic complaints)	21
Speech difficulties	19
Dizziness	18
Memory and intelligence deficit	18
Fainting	17
Character changes	15
General weakness and fatigue	14
Drowsiness	12
Loss of hearing	11
Incontinence	9
Weakness of facial muscles	9
Psychoses	8
Amenorrhea	5
Weakness of half of one side	5
Stiffness of neck	4
Weight loss	3
Tremor of hands	2
Tilting of head	1
Loss of sense of smell	1

Observations

Pathological Observations

The cases were chosen at random from the files of the Department of Pathology, the Department of Psychiatry and the Department of Surgery. Eighty per cent of the material came from patients who had died; 74 per cent of the patients had had craniotomies. The case records were collected from 1935–1944. The locations of these tumors are presented in Table 2. Their typing, following the customary outline of Cushing,[1] is presented in Table 3. The preponderance of malignant types reflects the fact that many of the cases were chosen from post-mortem files. Thus, this study is not characteristic of brain tumors as the neurosurgeon sees them but of patients with brain tumors who die. This actually represents patients in whom the process was more severe and in whom the symptoms were therefore probably more striking.

Table 2. *Locations of the Tumors.*

Location	No. of Cases
Temporoparieto-occipital	37
Frontal	24
Posterior fossa	23
Pituitary and hypothalamus	9
Basal ganglions	7
	100

Table 3. *Types of Tumors.*

Tumor	No. of Cases
Glioblastoma	46
Astrocytoma	12
Meningioma	11
Spongioblastoma (polare)	7
Craniopharyngioma	5
Chromophobe adenoma	3
Ependymoma	3
Medulloblastoma	3
Acoustic neuroma	2
Astroblastoma	2
Oligodendroblastoma	2
Sarcoma	2
Eosinophilic	1
Tuberculoma	1
	100

Diagnoses of the Community

Relatively little information was obtained regarding diagnoses by friends or relatives. It is of interest, however, that of the 16 recorded diagnoses personality disorders were mentioned in 10 cases and that 2 others were considered alcoholism because of the patients' drunken gait. Eye trouble was diagnosed in 2 cases, and epilepsy in one, and a chiropractor made 1 diagnosis of "misplaced axis."

Such diagnoses undoubtedly reflect to some degree the popular interest in nervous disorders and the opinion of many lay people that they are competent to diagnose and prescribe for such difficulties themselves.

Diagnoses by Family Physicians

About half the patients left their physicians presumably dissatisfied with the unsuccessful treatment and lack of diagnosis. The other half were eventually referred to hospitals because of "serious disease" requiring more careful and specialized study. The survey of these diagnoses is given in Table 4. Only 4 per cent correct diagnoses and 2 per cent doubtful diagnoses of brain tumor were made. It is interesting that patients reached specialists in most cases only after having been investigated by internists, surgeons, ophthalmologists and so forth, and in no case were they referred directly by general practitioners in the community.

TABLE 4. *Diagnoses by Medical Practitioners in the Community.*

DIAGNOSIS	NO. OF CASES
"Nothing wrong"	20
Emotional disorder (neurosis)	12
Epilepsy	5
Eye disease	5
Brain tumor	4
Suspicion of brain tumor	2
Cerebral accident	1
Appendicitis	1
Sinusitis	1
Facial palsy	1
Anemia	1
Psychosis	1
Rheumatic fever	1
Encephalitis	1
Neuralgia	1
Optic atrophy	1
Head injury	1

The low percentage of correct diagnoses may also have been influenced by the social group. The lay group tends to evaluate any deviation from the normal in terms of nonconformity with accepted patterns of behavior rather than in medical or physical terms.

Diagnoses Made in Hospitals by Nonspecialists

These diagnoses are given in Table 5. The percentage of correct diagnoses has increased considerably, being correct in 29 and at least considered in 8 additional cases. The diagnosis of personality disorder is still high, however (psychoneurosis, 13 cases, and psychosis, 2 cases), and 11 cases were listed as "no diagnosis." It is probable that in the last group there were many patients who were believed by the examining physicians to be psychoneurotic but on whom they were unwilling to make a definite statement. The diagnosis of epilepsy is still considered in an impressive number of patients.

Diagnoses Made by Neurologists, Psychiatrists and Neurosurgeons in Hospitals

Of the 100 patients 94 were seen by specialists, and in all but 7 cases the correct diagnosis of brain tumor was made. The signs observed on neurologic and psychiatric examination are presented in Table 6. In 5 patients — notably, those with personality disorders — the initial diagnosis made by a specialist was wrong, and observation and the help of another consultant facilitated the correct diagnosis. In 49 patients a correct localization was made, and in 28 patients a correct clinical diagnosis of the histologic type of tumor was made. Three cases in which diagnoses were missed by specialists are briefly reported below.

TABLE 5. *Diagnoses Made in Hospitals by Nonspecialists.*

DIAGNOSIS	NO. OF CASES
Brain tumor	29
Personality disorder	13
Epilepsy	13
No diagnosis	11
Cerebral arteriosclerosis	5
Eye disease (unspecified)	5
Hypertension	4
Cerebral accident	3
Optic atrophy	2
Encephalitis	2
Head injury	2
Psychosis	2
Diabetes insipidus	2
Multiple sclerosis	1
Meningitis	1
Hyperthyroidism	1
Central-nervous-system syphilis	1
Syringomyelia	1
Carcinoma of stomach	1
Degenerative brain disease	1

TABLE 6. *Signs Found on Neurologic and Psychiatric Examination.*

SIGN	NO. OF CASES
Papilledema	67
Reflex changes	59
Weakness of muscles enervated by cranial nerves, with exception of eye muscles	42
Symptoms pertaining to lesion of oculomotor nerves	41
Weakness of extremities and trunk	32
Disturbances of co-ordination	29
Speech disturbances (dysphasia, dysarthria and so forth)	19
Visual-field disturbances	18
Psychotic syndromes	15
Intellectual deficit	12
Personality changes (neurotic reactions and character changes)	10
Lesions of cranial sensory nerves	8
Symptom of cutaneous nerves, including deep pain	8
Loss of olfaction	7
Disturbance of consciousness	5
Meningeal signs	3
Forced grasping	2
General debility	1
Bony prominence of skull	1
Dullness, left forehead	1
Seizure observed	1

CASE 1 (A75793). A 72-year-old laborer entered the emergency room with a history of having "fainted" while descending the stairs and of having consequently struck his head and left arm. He also stated he had been treated by his family physician for years for a heart condition.

Physical examination was reported negative except for swelling of the left wrist, abrasion of the left side of the

face and head and auricular fibrillation and cardiac enlargement. X-ray study revealed a Colles fracture of the left wrist and a fracture of the left parietal bone. The patient was treated and discharged 12 days later.

After 3 weeks he was readmitted to the hospital because he had an episode of vomiting at midnight followed by a stool containing bright-red blood. Physical examination was essentially negative except for his cardiac status and the fact that he was noted to be "senile"; the fundi were "not well visualized." A positive Romberg test was noted. The diagnostic considerations were mainly concerned with the rectum.

Thirty-three days after admission the patient was observed one night to have a sudden drop in blood pressure. He perspired profusely, and yet the pulse remained full and strong; no temperature changes were noted. It was assumed that he had had a large hemorrhage into his bowel. The next morning he was observed to have a right-sided hemiparesis, a bilateral positive Hoffmann sign, right positive Babinski sign, absent superficial reflexes and drooping of the right corner of the mouth. The diagnostic assumption was that he had a cerebral hemorrhage. No lumbar puncture, electroencephalogram or air study was done. The patient's course was rapidly downhill, and he died 3 days later.

The post-mortem findings were meningioma, compressing the right motor strip, generalized arteriosclerosis with multiple hemorrhages in the small bowel and cardiac hypertrophy.

Case 2 (A53451). A 58-year-old housewife was first seen in the psychiatric inpatient service on March 7, 1935. The past history revealed that approximately 3 years previously she had noted a progressive failing of vision. Two years before admission tinnitus developed, and her appetite was no longer as good as it had been. Approximately 6 months later a left frontal headache developed, which was intermittent, and she began to fear being alone. This was followed by an attack of severe headache accompanied by nausea and vomiting and by several days of depression. She gradually became forgetful and depressed, and had some difficulty in speaking. At about this time her friends noticed personality changes, and two physicians believed that her difficulty was not organic. Six months later her vision became much worse and she was again seen by two physicians, one of whom made no diagnosis, and the other of whom treated her tinnitus with "electricity." Her speech became worse, and on consulting another physician she was referred to the psychiatric inpatient service.

On admission the provisional diagnosis was cerebral arteriosclerosis with encephalopathy. The positive neurologic signs were weakness of the right facial nerve, hyperactive deep tendon reflexes on the right, apraxia and a questionable right homonomous field defect. This was confirmed by neurologic consultation. Lumbar puncture disclosed a spinal-fluid pressure equivalent to 195 mm. of water, varying up to 235 mm. No other laboratory studies were done except for routine blood and urine examinations.

The patient died 2 days after admission.

Post-mortem examination revealed a glioblastoma multiforme involving the left temporoparietal lobe.

Case 3 (A70941). A 19-year-old boy was first admitted to New Haven Hospital (neurosurgical service) on August 13, 1942, because of severe frontal and occipital headaches on June 28. These were severe in the early morning, disappearing about 10 a.m. They became progressively worse, and nausea and vomiting appeared after 2 weeks. He complained of transient dizziness but no true vertigo. He had received his draft classification on June 30. The past history was otherwise irrelevant.

Physical examination was entirely negative, including neurologic examination, with the exception that he "staggered in all directions on walking." The diagnostic impression was "hysteria." The patient was noted to be of "low intelligence."

Lumbar puncture on the day after admission showed an initial spinal-fluid pressure equivalent to 110 mm. of water, with a protein of 82 mg. per 100 cc. On August 17 no pressure was noted; the protein was 42.5 mg. per 100 cc.

The patient was to have a skull x-ray film but this procedure was not done. He was discharged on August 17 with a diagnosis of hysteria. He was seen 1 month later in the clinic and at this time his symptoms were still present, and the diagnosis was the same; he was referred to the psychiatric outpatient clinic.

The patient was followed in the psychiatric outpatient clinic until November 10, when his symptoms became exacerbated and he was admitted to the psychiatric service. At this time he was described as being stuporous, dehydrated and acutely ill. He had cervical rigidity, suboccipital tenderness and a positive Kernig sign on the right. The pupils were dilated, the left one being sluggish to light. Bilateral papilledema (4 diopters), with hemorrhages, was noted. Dysarthria, left-facial-nerve weakness and bilateral ankle clonus were present.

Lumbar puncture on admission showed an initial spinal-fluid pressure equivalent to 350 mm. of water, with a total protein of 30 mg. per 100 cc. The diagnosis of an expansile lesion of the brain was made. The patient died on the night of admission.

Post-mortem examination on November 11 disclosed sarcoma of the left cerebellar hemisphere, with extension into the dura and fourth ventricle, atrophy of the sella and inner table of calvarium and a cerebellar pressure cone.

Diagnostic Contributions of Laboratory Technics

Cerebrospinal Fluid

Lumbar punctures were recorded on only 41 of the 100 patients. In 38 cases the cerebrospinal fluid was abnormal, and the test confirmatory. In 36, the pressure was over 180 mm. of water. The total protein was above 50 mg. per 100 cc. in 24 patients. In 5 cases no attention was paid to the abnormal spinal-fluid findings, and thus a very important clue to the diagnosis of brain tumor was missed.

Radiologic Examination of the Skull

In 91 patients x-ray films of the skull were taken. This probably reflects the ease of ordering skull films and the prominence of radiologic diagnosis in general medical thinking. In contrast to the high percentage of positive spinal-fluid findings, however, pathologic findings were noted in only 48 cases. In only 2 cases did the x-ray examination lead to erroneous localization.

Electroencephalogram

Since many patients were examined before the electroencephalic laboratory was organized, electroencephalic reports were available in only 21 patients; 19 of these were abnormal, indicating a significant contribution to diagnosis. In 10 of these patients the lesion was localized by the electroencephalogram.

Ventriculogram

Ventriculograms were performed in 33 patients. Localization was correct in 27 cases — a significant proportion. In 2 patients the localization was false.

Delays in Diagnosis

The number of months elapsing between the first time when a diagnosis seemed possible and the moment of correct diagnosis was estimated. The mean of such delay was fifteen months, the median twenty-four, and the longest interval eighteen years.

In a third of all patients, the time loss was less than three months, however, and in half the cases the time loss was less than one year. Because the delay in the more malignant groups is necessarily low, the time loss in the less malignant tumors seems even more striking.

Diagnostic errors made during the period of hospitalization are presented in Table 7. In some of these cases the correct diagnosis was missed owing to a combination of errors. For example, under the heading of inadequate neurologic examination, both lack of a reasonably thorough examination and a gross lack of interpretation of positive neurologic signs are included.

Discussion

In about half the patients the diagnosis of brain tumor was seriously delayed (over one year). In almost a fourth of these patients the delay was more than two years. Much of this was due to ignorance and inertia on the part of the patients' families, who did not consult a physician. On the other hand, of course, it is a common experience of many psychiatrists to see patients suffering from fatigue, giddiness and mild headaches who hypochondriacally assume the diagnosis of brain tumor. On the basis of knowledge of initial signs and symptoms it should be possible to stress the need for medical examination in the presence of headaches, visual impairment and giddiness accompanied by nausea. Education along this line need not remark on the possibility of brain tumor, but only on the necessity for seeking medical advice.

The low percentage of correct diagnoses of brain tumors by general practitioners in the community is striking. This is offset by the fact that about half the patients in whom no appreciable time loss in diagnosis occurred (a sixth of all patients) went through the hands of physicians in the community. An even higher percentage of the total number of patients was referred to hospitals or to other specialists with the diagnostic assumption by the general practitioner of a severe illness requiring more thorough diagnostic study.

In the face of these referrals the question arises why the diagnosis of brain tumor is missed at this early stage. Is this due to unawareness of the signs and symptoms of brain tumor, or to failure to carry out necessary examinations? It is our impression that the most important considerations are pressure of time and certain characteristics of a general medical practice that lead to errors or to omissions. One factor determining this may be the reluctance of physicians practicing in certain social groups to diagnose such illnesses as tumors because of the tendency of patients to blame the physician for the consequences of the disease. This also holds for such diagnoses as "tuberculosis" and "mental illness." More important, however, is the probability that many more correct diagnoses could have been made if a cursory neurologic examination aimed at the detection of muscular weakness, reflex changes and visual symptoms and signs had been performed. The most important of these is an ophthalmoscopic examination. The question then is, Why do general practitioners not carry out such neurologic examinations including ophthalmoscopy? The following possible factors suggest themselves: insufficient emphasis in medical training on important practical steps in diagnosis and treatment, such as the carrying out of a brief "emergency neurologic examination"; insufficient reward in the way of positive findings seems to result in the abandonment of such special examinations as ophthalmoscopy by general practitioners — this may explain to some degree why general practices are often considered dull in terms of detection and treatment of rare diseases; the tendency to attribute symptoms to minor neurotic difficulties is strikingly dramatized by the diagnosis of "nothing wrong" in 20 of the 49 diagnoses made by local practitioners and of a personality difficulty in 12 cases. The proportion so diagnosed (54 per cent) was markedly reduced by the nonspecialists' diagnoses made in hospitals (24 per cent). Since a review of early complaints reveals psychiatric and neurologic symptoms or intellectual deficit in 41 patients, the error obviously consists not in assuming personality disorders when they are absent but in neglecting to find the proper cause for such disorders. The simple device of looking for behavioral disorder and organic signs and then correlating both should help to avoid this frequent error.

Table 7. *Survey of Diagnostic Errors in Hospitals.*

Error	No. of Cases
Inadequate neurologic history and examination	27
False evaluation of personality disorder	15
Seizures not explored	14
Headaches not evaluated	8
Failure to evaluate visual symptoms	6
Failure to evaluate cerebrospinal-fluid findings	5
Insufficient laboratory work	5
History of head injury overevaluated	4
Overevaluation of hypertension	4
Assumption of degenerative brain disease based on insufficient evidence	4
Examiner sidetracked by medical symptoms (elevated temperature, glycosuria, hyperthyroidism)	3
Overevaluation of alcoholic history	2
Coma not investigated	1
Deafness not investigated	1
Too great dependence on negative laboratory findings	1

Hospital physicians have the advantage of observing changes in the patient over a period and in addition, early technics for refined diagnoses are more available. Still, inadequate neurologic examinations and false interpretations of data were very important causes of errors. The lack of investigation of seizures was noteworthy. Symptoms such as these, as well as headaches and visual impairment, were often easily assumed to be due to hypertensive encephalopathy, cerebral arterio-

sclerosis and various progressive degenerative brain diseases.

Compared with other groups, the percentage of correct diagnoses made by specialists (neurologists, neuropsychiatrists and particularly neurosurgeons) was high. This demonstrates that available technics and knowledge permit a high degree of diagnostic acumen. On the other hand, it must not be overlooked that previous spade work helps greatly to eliminate errors, and, in addition, it is always easier to diagnose tumors in later stages than at the onset.

Laboratory procedures appeared to have mostly confirmatory value rather than to be useful as independent diagnostic technics. Clinical findings seem to be of primary importance. The early use of radiologic and electroencephalographic technics, however, is highly recommended, and it is our impression that the electroencephalogram is by no means as frequently used as it should be. Lumbar puncture in persons suspected of having tumors seems best reserved for hospital practice. The possible development of a pressure cone, particularly in posterior-fossa tumors, should be seriously considered. Air studies in most cases are late studies to establish localization and should be done only by neurosurgeons equipped to follow through with operation if necessary.

On the basis of the above material, a recommendation for better mass health education regarding early symptoms of dangerous disease — in this case, of tumors and particularly of brain tumors — seems justified. This is an exceedingly delicate problem, however, and a great deal of thought is necessary to spread knowledge on a mature, realistic level without increasing general hypochondriacal concern. Possible agencies of communication are biology classes in school, health drives, appropriate literature and radio talks.

At the level of the physician, teaching of abbreviated neurologic examinations in medical schools and hospitals might decrease the incidence of error and delay in the diagnosis of brain tumor. The principle of appropriate referral to specialists when the practitioner is unable to carry out the necessary examinations needs a more liberal and intelligent interpretation. Attention should be drawn to statistical tables demonstrating early signs and symptoms. Certain general diagnostic procedures — for example, ophthalmoscopy — seem so basic that they should not be abandoned even under the pressure of a busy practice, or if negative findings are obtained in an overwhelming number of cases. Such frequent diagnostic errors as failure to explore seizures, headaches and visual impairment, failure to examine for changes in the fundi, slight muscular weaknesses and reflex changes can be avoided. Personality changes should be explored from both an organic and a behavioral point of view and should not be used in themselves as an excuse for cessation of further organic or behavioral investigation. Results of laboratory procedures should be used and interpreted within the context of the total clinical situation. Thus, achievements so far the prerogative of the specialist will find a wider and more useful application in the field of general medical practice.

Summary

A study of 100 proved cases of brain tumor revealed that in approximately half the cases the diagnosis was delayed for a year or longer. Although social and psychologic factors often delayed referral by the family to a physician, the low percentage of correct diagnoses by practitioners in the community was striking. The failure of the practitioner to carry out routine brief neurologic examination and a tendency to attribute symptoms to personality difficulties with subsequent lack of further investigation seem important. A standard survey of early signs and symptoms and errors due to overlooking or ignoring of such findings is made. The value of specific clinical and laboratory studies is assessed. Public-health education designed to avoid such delays in diagnosis is indicated at both lay and professional levels.

References

1. Horrax, G. Diagnosis and prognosis of brain tumors. *Bull. New York Acad. Med.* **19**:125-131, 1943.
2. McIntyre, H. D., and McIntyre, A. P. Problem of brain tumor in psychiatric diagnosis. *Am. J. Psychiat.* **98**:720-726, 1942.
3. Purves-Stewart, J. Clinical study of intracranial tumours and especially of errors in their diagnosis. *Proc. Roy. Soc. Med.* (Sect. Neurol.) **20**:1-8, 1926.
4. Hastings, D. W. Difficulties in differential diagnosis of brain tumor in older age groups. *J. Nerv. & Ment. Dis.* **89**:44-51, 1939.
5. Bing, R. Tumeur cérébrale à symptomatologie fruste. *Schweiz. Arch. f. Neurol. u. Psychiat.* **33**:219-227, 1934.
6. Poppen, J. L., and Peacher, W. G. Brain tumors in presence of normal air studies. *S. Clin. North America* **23**:803-813, 1943.
7. Cushing, H. *Intracranial Tumours: Notes upon a series of two thousand verified cases with surgical-mortality percentages pertaining thereto.* 150 pp. Springfield, Ill.: Charles C Thomas, 1932. Pp. 8 and 11.

THE EFFECT OF SUBACUTE BACTERIAL ENDOCARDITIS ON THE COURSE OF THE UNDERLYING HEART DISEASE*

BERNARD RAPOPORT, M.D.,† AND LAURENCE B. ELLIS, M.D.‡

BOSTON

THE development of a successful treatment for subacute bacterial endocarditis by penicillin has greatly changed the significance of this condition as an event in the life history of a person with chronic heart disease. Formerly, the disease was almost universally fatal, with the infection itself dominating the clinical picture, and therefore it was of relatively little moment whether heart failure developed or not. Now, since the infection can usually be controlled, if increased cardiac damage occurs it may materially increase the disability or lead to early death of the patient from heart failure. Many of the investigators[1–12] who have reported the results of the penicillin treatment of patients with subacute bacterial endocarditis have emphasized both the importance of heart failure or acute cardiac accidents as a factor in a fatal outcome during treatment, and the development of increased cardiac disability following successful arrest of the infection. It is not apparent in most of the reports to what extent decreased cardiac reserve was present in patients before the infection developed or treatment was begun. Fiese,[11] however, made a careful study of the factors responsible for cardiac failure developing after treatment and concluded that this condition is the result of a number of factors, no one of which is exclusively responsible. The most important are the previous reserve and size of the heart, the patient's age, the type of lesion of the heart, the height of the temperature, the general clinical appearance, and the length of time before adequate treatment. Jones et al.[12] have reported a detailed follow-up study. These authors found that although the patients who recovered claimed no subjective increase in disability they often presented objective evidence of increased cardiac damage as evidenced by progressive cardiac enlargement. When the data are given in the case reports of these and other authors it is evident that heart failure developed a few weeks after the conclusion of treatment.

The purpose of the present study was to assess the late results of subacute bacterial endocarditis on the cardiac status of patients. Hence we selected a group of patients who were treated a minimum of two years before the follow-up studies.

MATERIAL

The material for this report consists of 15 patients with subacute bacterial endocarditis caused by alpha-hemolytic streptococcus who were treated at the Boston City Hospital during 1944 and 1945, and comprises the total number of such cases seen at the institution during this period satisfying the following criteria. Cases were accepted that had at least two positive blood cultures for *Streptococcus viridans* and had clinical evidence of valvular heart disease. All but one of the patients gave evidence of peripheral emboli. Four of the 15 patients have died, and the diagnosis of subacute bacterial endocarditis was confirmed in each case by post-mortem examination. All the living patients were reexamined two years or later after their original infection by one of us (B. R.) in June, 1947. Complete blood counts, urinalyses and blood cultures were done, and teleroentgenograms of the heart and electrocardiograms were taken. The relevant findings are shown in Tables 1 and 2.

Age and Sex

There were 5 male and 10 female patients. The ages ranged from nineteen to sixty years. Of the 4 patients who died, 2 were men aged forty-nine and fifty-three, and 2 were women aged twenty and twenty-one.

Etiology of Heart Disease

In all cases the clinical diagnosis was chronic rheumatic heart disease. This was confirmed at autopsy in the 4 fatal cases. In 8 of the 15 patients no preceding history of rheumatic fever could be obtained; in the remainder there were definite histories of rheumatic fever.

Valvular Involvement

In the 11 living patients evidence of involvement was limited to the mitral valve in 7 cases, and in the other 4 there was evidence of disease of both mitral and aortic valves at the time of treatment for subacute bacterial endocarditis. When follow-up examinations were done, signs of valvular deformities had remained unchanged in all cases. In the fatal cases clinical examination indicated mitral and aortic involvement in 2, and mitral involvement alone in 2. At post-mortem examinations the clinical diagnosis was confirmed in 3, and

*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

†Formerly, resident fellow in medicine, Harvard Medical School; formerly, assistant in medicine, Boston City Hospital; formerly, resident fellow, Thorndike Memorial Laboratory, Boston City Hospital.

‡Assistant clinical professor of medicine, Harvard Medical School; assistant visiting physician, Boston City Hospital; associate physician, Thorndike Memorial Laboratory, Boston City Hospital.

in a case suspected clinically of mitral valvular disease alone there was evidence of healed aortic valvulitis of rheumatic etiology as well. The bacterial vegetations involved only the mitral valve in this case.

Heart Size

The heart size was obtained from 6-foot teleroentgenograms. Slight changes in serial measurements, which could have been due to altered position of the heart in the chest, were disregarded. The degree of cardiac enlargement was classified as "none," "moderate" or "marked." There was evidence of marked cardiac enlargement in 3 of the fatal cases when the patients were admitted for treatment of bacterial endocarditis. In the other fatal case no enlargement was noted. In 4 of the 11 living patients there was marked enlargement at the time of treatment, and on follow-up examination the same degree of enlargement was found. Six showed moderate enlargement during their infection, and in 4 of these on the follow-up examination the hearts were normal in size clinically and by x-ray examination, and 2 remained unchanged. One patient showed no definite cardiac enlargement at any time, but x-ray examination during the infection showed some straightening of the left border of the heart, which was unchanged two years later.

Rhythm

All the patients in this series had sinus rhythm when admitted for treatment. One (Case 11) developed auricular fibrillation during the active infection and reverted to sinus rhythm on quinidine therapy. Another (Case 3) has developed persistent auricular fibrillation since being cured of his endocarditis, and his rate has been well controlled on digitalis therapy.

TABLE 1. *Cardiac Status during Infection and at Follow-up Examination.*

Case No.	Sex	Age	Valves Involved	Status of Cardiac Function		
				Before Infection	During Infection	At Follow-up Examination
		yr.				
1	F	45	Mitral Aortic	II	II	II*
2	F	22	Mitral Aortic	II	II	II
3	M	43	Mitral	II*	II*	II*
4	F	22	Mitral	II	II	II
5	F	28	Mitral Aortic	II	II	II
6	F	42	Mitral	I	I	I
7	M	28	Mitral Aortic	II	II	II
8	M	60	Mitral	I	I	I
9	F	19	Mitral	I	II	I
10	F	31	Mitral	I	IV	I
11	F	42	Mitral	II	III	II
12	M	53	Mitral Aortic	I	I	Patient died on 15th day of treatment
13	F	21	Mitral Aortic	I	II	Patient died on 6th day of treatment
14	M	49	Mitral Aortic	II	III	Patient died 3 months after treatment
15	F	20	Mitral	I	IV	Patient died 8 months after treatment

*Patient given digitalis.

Electrocardiographic Findings

The results of comparison of electrocardiograms recorded at the start of treatment for bacterial endocarditis and those taken on follow-up study are presented in Table 1. Records were available for comparison on all patients who survived except 1 (Case 5). In 8 cases there was no significant change. One patient developed auricular fibrillation, and in one the T waves in Leads 1 and 2 became inverted.

Cardiac Reserve

In Table 1 the functional capacity in each case is shown before, during and two to three years after the infection, rated in accordance with the classification of the American Heart Association.[13] In 3 living patients (Cases 9, 10 and 11) there was clinical evidence of decrease in cardiac reserve occurring during the febrile illness, and in 1 of these the transient auricular fibrillation occurred. In another patient (Case 10), in whom signs of cardiac decompensation were most marked and required physical signs of congestive heart failure. She was improved by digitalis and has continued on it, leading a fairly active life, and working twenty hours a week as a saleswoman in a department store.

All 11 patients, when examined in June, 1947, reported themselves to be at least as well as they had been before their illness. They were all as active as they had been in the years immediately prior to their subacute bacterial endocarditis, and in some cases stated that they could do more than they had been able to do before their illness. In

TABLE 1 (*Continued*).

Case No.	Rhythm		Cardiac Enlargement		Electrocardiographic Changes
	during infection	at follow-up examination	during infection	at follow-up examination	
1	Normal sinus rhythm	Normal sinus rhythm	Moderate	Moderate	No change
2	Normal sinus rhythm	Normal sinus rhythm	Marked	Marked	No change
3	Normal sinus rhythm	Auricular fibrillation	Marked	Marked	None, except auricular fibrillation
4	Normal sinus rhythm	Normal sinus rhythm	Moderate	None	No change
5	Normal sinus rhythm	Normal sinus rhythm	Moderate	Moderate	No record during infection
6	Normal sinus rhythm	Normal sinus rhythm	None	None	No change
7	Normal sinus rhythm	Normal sinus rhythm	Marked	Marked	Inversion of T waves
8	Normal sinus rhythm	Normal sinus rhythm	Moderate	None	No change
9	Normal sinus rhythm	Normal sinus rhythm	Moderate	None	No change
10	Normal sinus rhythm	Normal sinus rhythm	Moderate	None	No change
11	Normal sinus rhythm with transient auricular fibrillation	Normal sinus rhythm	Marked	Marked	No change
12	Normal sinus rhythm	—	None	—	—
13	Normal sinus rhythm	—	Marked	—	—
14	Normal sinus rhythm	—	Marked	—	—
15	Normal sinus rhythm	—	Marked	—	—

vigorous therapy with oxygen and digitalis, the heart failure was precipitated by the combination of the infection and the pregnant state, since her infection and her heart failure became manifest in the early puerperium. All 3 of these patients improved after treatment to a point where their cardiac reserve was as good as that before the infection developed.

One patient who did not develop any signs or symptoms of heart failure during treatment for endocarditis was started on digitalis therapy about ten months later because of the complaint of dyspnea although the degree of shortness of breath had not increased. At this time there were no

none of these patients were there any clinical or urinary findings suggesting chronic renal disease.

It will be noted that there was a diminution in cardiac reserve in 3 of the fatal cases associated with the infection and that in the fourth case no change was noted. In 3 of these cases there was evidence of persistent active bacterial infection at autopsy, and thus they represent failures in the treatment of the infection. One patient (Case 15), who developed the most marked cardiac failure during her infection, was cured of the infection and died of a coronary embolus eight months after the eradication of the infection. During this period she remained in severe heart failure, requiring digi-

talis and frequent mercurial diuretics. The case history of this patient is as follows:

A 20-year-old woman was first admitted to the hospital on June 16, 1945, with a history of chills, fever and headache of 11 days' duration and a history of a known heart murmur for 4 years. There was no history of rheumatic fever or cardiac disability. She was found on this admission to have a meningococcal (Group I) infection of the blood and spinal fluid. She was successfully treated with sulfadiazine and penicillin, with rapid improvement and was discharged as cured after 8 hospital days. Cardiac examination during this admission showed a heart that was enlarged, the border of cardiac dullness extending to the left anterior axillary line, and there was a loud, harsh apical systolic murmur. There was no evidence of cardiac decompensation.

She was readmitted to the hospital 5 months later, with a 2-month history of night sweats, anorexia and malaise and a 3-week history of cough and some dyspnea on exertion. On entry she was febrile, no petechiae were noted on the skin, and the lungs were clear. The heart was enlarged, with a rapid regular rhythm, the sounds were of good quality, and there was a loud apical systolic murmur with a palpable thrill. The spleen was palpable. There was minimal pitting edema of both ankles, and questionable clubbing of the fingers. Roentgenographic examination of the chest showed cardiac enlargement and congestive changes in both lung fields. Three positive blood cultures for *S. viridans* were obtained, and 2 days after admission petechiae were noted in the left conjunctiva and a diastolic murmur was heard at the apex. Treatment with penicillin (30,000 units intramuscularly every 3 hours) was begun on December 3, and continued until December 28. No positive blood cultures were obtained after December 3, and the temperature remained normal after discontinuation of therapy. However, tachycardia persisted and because of persistent signs of cardiac decompensation, digitalis and diuretic therapy was begun. The patient remained in the hospital until February 13, 1946, when she was discharged home still showing signs of cardiac failure. She remained home under the care of a private physician in chronic heart failure until 6 months after discharge, when she was readmitted to the hospital complaining of chilly sensations and an acute severe knifelike substernal pain radiating through to the back and aggravated by respiration.

Physical examination revealed her to be cyanotic, and the extremities were mottled, blue and cold; no pulses could be obtained in the fect, and the radial pulses were rapid and thready. The lungs were clear, the heart was enlarged, the border of cardiac dullness extending to the anterior axillary line in the fifth left interspace, the rate was 100, and the rhythm was irregular; a loud apical systolic murmur was present, and there was a moderately loud apical presystolic murmur. A moderately loud systolic murmur was heard in the aortic area. The liver edge was palpable six fingerbreadths below the costal margin. There was minimal clubbing of the fingers; no pitting edema was noted. The patient failed to respond to therapy and died a few hours after admission.

At autopsy on the following day the heart appeared grossly enlarged, weighing 450 gm., and the left auricle was moderately dilated. The epicardium was not remarkable, and the endocardium was not remarkable except for the left auricle and the mitral valve. On the wall of the auricle there were many somewhat orange-tinged plaques of elevation, which were glairy in appearance and seemed to be part and parcel of the auricular wall. On the margin of the aortic cusp of the mitral valve, which was somewhat thickened, there were many yellowish irregular glistening masses, and three or four of the chordae tendineae enmeshed in these masses seemed to have been ruptured and healed on the surface. Lodged in the orifice of the right coronary artery there was a mass of material resembling the vegetations on the mitral valve. This completely occluded the orifice, and distally the artery was filled with a recent thrombus. The remainder of the valves and the left coronary artery were not remarkable. There was an area in the center of the base of the interventricular septum that appeared to be slightly yellowish red and mottled. Microscopically, the endocardium of the left auricle showed regions of subendocardial fibrous thickening. The myocardium disclosed focal fibrosis, most marked in perivascular locations. A section from the center of the interventricular septum demonstrated more marked fibrosis than in the ventricular wall, and a section from near the septum at the junction of the left auricle and left ventricle showed areas of polymorphonuclear-leukocyte infiltration between the muscle fibers. Culture from the mitral valve was negative for streptococcus with alpha hemolysis. The final pathological diagnoses were: rheumatic heart disease, old, with mitral insufficiency; cardiomegaly; myocardial fibrosis; healed bacterial endocarditis, with rupture of chordae tendineae of the mitral valve; vegetations on mitral valve; embolus in orifice of right coronary, with myocardial infarction; healed infarcts in spleen and kidney; focal embolic glomerulonephritis, healed; chronic passive congestion of liver, spleen, kidneys and gastrointestinal tract; ascites; and bilateral hydrothorax.

TABLE 2. *Penicillin Treatment of 15 Patients with Subacute Bacterial Endocarditis.*

CASE NO.	TIME FROM FIRST SYMPTOM TO END OF PENICILLIN TREATMENT	TOTAL DOSE OF PENICILLIN	DURATION OF TREATMENT	METHOD OF ADMINISTRATION	OUTCOME
		units	*days*		
1	8 wk.	4,200,000	16	Intermittent intramuscular	Patient living
2	4 wk.	5,670,000	20	Intermittent intramuscular (heparin given intravenously for 12 days)	Patient living
3	10 wk.	5,895,000	19	Intermittent intramuscular and continuous intravenous	Patient living
4	9 wk.	3,555,000	13	Intermittent intramuscular	Patient living
5	4 mo.	5,725,000	21	Intermittent intramuscular	Patient living
6	4 wk.	5,460,000	22	Continuous intramuscular	Patient living
7	24 mo.	3,700,000	14	Intermittent intramuscular	Patient living
	(3 recurrences)	6,265,000	22	Intermittent intramuscular and continuous intravenous	Patient living
		10,980,000	38	Intermittent intramuscular and continuous intravenous	Patient living
		33,000,000	50	Continuous intravenous	
8	14 mo.	4,225,000	12	Intermittent intramuscular	Patient living
	(2 recurrences)	5,100,000	15	Intermittent intramuscular	
		9,600,000	33	Intermittent intramuscular	
9	8 wk.	5,600,000	21	Continuous intramuscular	Patient living
10	12 wk.	3,010,000	14	Intermittent intramuscular	Patient living
11	4 mo.	6,120,000	25	Continuous intramuscular and intravenous intramuscular	Patient living
12	9 wk.	4,525,000	15	Intermittent intramuscular .	Patient dead
13	4 wk.	1,865,000	6	Intermittent intramuscular	Patient dead
14	8 mo.	4,200,000	16	Intermittent intramuscular (heparin intravenously for 5 days)	Patient dead
15	12 wk.	6,080,000	25	Intermittent intramuscular	Patient dead

Cardiac Status

In 5 cases data were available to permit some comparison of the cardiac status before the development of the bacterial endocarditis with later findings. One patient (Case 15) had developed

progressive cardiac failure after cure of the infection and died of a coronary embolus eight months later. In this case the marked enlargement of the heart and harsh apical systolic murmur, which was present when treatment was started, had also been noted five months earlier. In the 4 other cases (Cases 3, 4, 7 and 9) the cardiac findings noted at the time of admission with the bacterial infection had been present in the same degree on previous examinations made two, six, ten, and five years earlier respectively.

Treatment

Table 2 contains a summary of the treatment with penicillin in all cases. Several of these cases have previously been reported.[14] These patients were treated when penicillin supplies were scarce, and the dosages were somewhat lower than those used in the treatment of this disease at present. In most cases the daily dose was between 200,000 and 300,000 units of penicillin.

Discussion

Subacute bacterial endocarditis can increase cardiac damage in spite of cure of the infection either by causing rupture of a valve cusp or of chordae tendineae, or by the later scarring and distortion of the valves resulting from the healing and absorption of vegetations producing increased mechanical inefficiency of the heart. The effects may be severe, with rapidly developing heart failure, especially when there is great destruction of a valve.[1, 2, 12] Such failure develops during or soon after the active infection. Several observers have commented on the development of failure of this type particularly when the aortic valve is involved.[6, 14] The late development of a diminished cardiac reserve is in many cases related to the scarring process.

Heart damage accompanying subacute bacterial endocarditis may also be produced by acute myocardial lesions. It has been observed that the hearts of patients dying of subacute bacterial endocarditis very commonly show histologic evidence of myocarditis, especially small infarcts[15] due to minute coronary emboli.[16] Such lesions may well be an important factor in heart failure developing during or shortly after the active infection, and the myocardial fibrosis that may follow could be a contributory element in a later decrease in cardiac reserve.

In our series there was no correlation between the development of cardiac failure and the age of the patient or the length of time the infection had persisted prior to the successful treatment. This is shown most obviously in the 2 patients with relapses, who had recurrent and probably persistent active endocarditis for more than twenty-four and fourteen months. One of the patients (Case 8) was sixty years old, and his heart was actually smaller two years after his cure. The other (Case 7) had cardiac enlargement with free aortic regurgitation when he first came under observation, which had not demonstrably changed nearly three years later.

Summary

Fifteen cases of subacute bacterial endocarditis caused by streptococcus with alpha hemolysis, which were treated in 1944 and 1945 and reexamined in June, 1947, at least 2 years after the original infection, are reported.

Eleven patients were living and well. Subjectively they all felt as well as they had prior to their infection. In 4 patients the cardiac size decreased after cure of the infection; in the other 7 there was no change. One had developed auricular fibrillation, and another has been taking digitalis for dyspnea although it is not clear that her condition has changed materially. In another patient the electrocardiogram showed evidence suggesting an increase in myocardial damage. These changes could as well have been due to the inevitable course of rheumatic heart disease in general as to any specific effect of the bacterial endocarditis.

Four patients in the group had died and were autopsied. In 3 there was post-mortem evidence of persistent active infection. One patient died in spite of eradication of the infection. Death in this case was due to a coronary embolus, but the patient had been in chronic congestive failure since cure of the infection.

References

1. Rosenblatt, P., and Loewe, L. Healed subacute bacterial endocarditis. *Arch. Int. Med.* **76**:1-10, 1945.
2. Bloomfield, A. L., and Halpern, R. M. Penicillin treatment of subacute bacterial endocarditis: some problems. *J. A. M. A.* **129**:1135-1141, 1945.
3. White, P. D., Mathews, M. W., and Evans, E. Notes on treatment of subacute bacterial endocarditis encountered in 88 cases at Massachusetts General Hospital during six-year period 1939 to 1944 (inclusive). *Ann. Int. Med.* **22**:61-74, 1945.
4. Dawson, M. H., and Hunter, T. H. Treatment of subacute bacterial endocarditis with penicillin: results in 20 cases. *J. A. M. A.* **127**: 129-137, 1945.
5. Flippin, H. F., Maycock, R. L., Murphy, F. D., and Wolferth, C. C. Penicillin in treatment of subacute bacterial endocarditis: preliminary report on twenty cases treated over one year ago. *J. A. M. A.* **129**:841-843, 1945.
6. Mokotoff, R., Brams, W., Katz, L. N., and Howell, K. M. Treatment of bacterial endocarditis with penicillin: results of 17 unselected cases. *Am. J. M. Sc.* **211**:395-416, 1946.
7. Glaser, R. J., Smith, R. O., Harford, C. G., and Wood, W. B., Jr. Treatment of bacterial endocarditis with penicillin. *J. Lab. & Clin. Med.* **31**:291-312, 1946.
8. Favour, C. B., Janeway, C. A., Gibson, J. G., II, and Levine, S. A. Progress in treatment of subacute bacterial endocarditis. *New Eng. J. Med.* **234**:71-77, 1946.
9. Dawson, M. H., and Hunter, T. H. Treatment of subacute bacterial endocarditis with penicillin: second report. *Ann. Int. Med.* **24**: 170-185, 1946.
10. Honigman, A. H., and Karns, J. R. Healed subacute bacterial endocarditis: report of two cases with death due to congestive heart failure. *Ann. Int. Med.* **26**:704-712, 1947.
11. Fiese, M. J. Cardiac failure in penicillin-treated subacute bacterial endocarditis. *Arch. Int. Med.* **79**:436-448, 1947.
12. Jones, A. M., Herring, R., Langley, F. A., and Oleesky, S. Penicillin treatment of subacute bacterial endocarditis. *Brit. Heart J.* **9**: 38-64, 1947.
13. DeGraff, A. C., et al. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart.* Fourth edition. 282 pp. New York: New York Heart Association, 1939.
14. Meads, M., Harris, H. W., and Finland, M. Treatment of bacterial endocarditis with penicillin; experiences at Boston City Hospital during 1944. *New Eng. J. Med.* **232**:463-474, 1945.
15. Saphir, O. Myocardial lesions in subacute bacterial endocarditis. *Am. J. Path.* **11**:143-156, 1935.
16. deNavasquez, S. Incidence and pathogenesis of myocardial lesions in subacute bacterial endocarditis. *J. Path. & Bact.* **49**:33-38, 1939.

GENERALIZED BULLOUS ERUPTION FOLLOWING TESTING FOR SULFONAMIDE HYPERSENSITIVITY*

DAVID A. STRAUS, M.D.†

CHAMBLEE, GEORGIA

ERYTHEMA multiforme exudativum is a well recognized clinical entity, but despite extensive investigation its etiology is obscure.[1-4] Eruptions due to drug idiosyncrasy, which are compatible with the clinical picture of erythema multiforme exudativum, are not uncommon and have frequently been described.[5-12] The sulfonamides are among the drugs that have been incriminated.[5-9] There is no real agreement, however, regarding whether such an eruption, although morphologically and clinically indistinguishable from the idiopathic erythema multiforme exudativum, should be classified as truly part of the syndrome.[2, 4] Regardless of how this drug reaction is classified, the importance of establishing or excluding the sulfonamides as etiologic agents when the possibility of their future therapeutic use is considered can easily be appreciated.

Recently, a patient whose clinical course fulfilled the criteria of erythema multiforme exudativum was observed. In an attempt to establish the etiology of the syndrome the passive transfer test, as described by Leftwich,[13] was used. Because an atypical and severe reaction ensued after what is usually regarded as a benign test and because the observed phenomena reproduced the picture of erythema multiforme exudativum, it is thought desirable to call attention to the reaction.

CASE REPORT

J. W., a 31-year-old Negro sawmill laborer, had a history of having received in 1943 a course of antisyphilitic therapy consisting of 19 intravenous injections of an arsenical and 20 intramuscular injections of a bismuth compound. In 1945 there was a history of his being seen in a public-health center, where diagnoses of "early latent syphilis" and "erythema multiforme" were made and he was given 1,200,000 units of penicillin, 300 mg. of arsenoxide and 60 mg. of bismuth subsalicylate during a 10-day period. Nothing further could be learned about his condition at that time. On December 2, 1947, he was admitted to a state venereal-disease-treatment center with a penile ulcer of 1 year's duration and a pruritic rash between his toes. Negative serologic tests for syphilis were obtained from the blood and spinal fluid, and diagnoses of "chancroid" and "scabies" were made. He was given sulfathiazole orally and treated with an "antiscabetic routine" — the medication used in the latter was not ascertained. Two days later, after having received 2 gm. of sulfathiazole, he had an epileptiform convulsion, and the temperature rose to 103.8°F. (It was learned subsequently that he had had similar convulsive seizures about twice yearly since a head injury incurred at the age of 14.) The temperature remained elevated, and on the next day, ulcerated lesions appeared on the mucous membranes of the mouth. The sulfathiazole was discontinued. On the following day, flaccid bullae appeared on the extremities, and on the next day, on the eyelids, buttocks, penis and scrotum. He was given 300,000 units of penicillin in oil and beeswax daily, as well as intravenous fluids. He was transferred to Lawson Veterans Administration Hospital on December 28, 1947, with the diagnosis of "pemphigus."

Physical examination showed an acutely and severely ill patient. Swallowing was painful, and was possible only with liquids. The mucous membranes of the mouth and lips were

FIGURE 1. *Site of the Bullous Eruption Where Most of the Bullae Had Ruptured, Leaving a Raw Granulating Surface.*

*From the Medical Service, Lawson Veterans Administration Hospital, Chamblee, Georgia, and the Department of Medicine, Emory University School of Medicine, Atlanta, Georgia.

Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

†Resident in medicine, Lawson Veterans Administration Hospital.

raw and bleeding, and there were numerous, small bullae on the tongue. There were marked scleral injection and chemosis and a moderate amount of milky conjunctival suppuration. A few coarse inspiratory and expiratory rhonchi were heard scattered throughout the lung fields, which were otherwise normal. The skin of the entire body exhibited numerous bullae. These were varied in size, but most were of the size and shape of Brazil nuts. They were located superficially in the skin and most of them had been ruptured and part of the clear serous fluid evacuated, leaving a thin, loose membrane over their surface and giving the bullae a flaccid appearance. The surface skin of many of the bullae was absent, leaving a red, granulating, moist area (Fig. 1). There was no inflammatory reaction surrounding the bullae. The face was clear except for a bullous eruption on the upper eyelids and ears and the lip lesions described above. The entire surface of the palms and soles was covered by a large bullous formation (Fig. 2). The patient exhibited a balanitis, and there were small, denuded areas on the penis and scrotum (Fig. 3). There was a moderate, generalized lymphadenopathy. The spleen was not palpable.

The temperature was 101.2°F., the pulse 96, the blood pressure 100/50, and the respirations rapid, shallow and grunting.

Examination of the blood disclosed a hemoglobin of 15 gm. (Klett method) and a white-cell count of 7450, with 58 per cent neutrophils, 36 per cent lymphocytes, 1 per cent monocytes and 5 per cent eosinophils. Serologic tests for syphilis yielded three "doubtful" Kahn reactions and a negative Wassermann reaction. Urinalysis showed a +++ test for albumin and innumerable erythrocytes in the sediment. The erythrocyte

FIGURE 2. *Large Bullous Formation on the Feet, Which Was Even More Extensive over the Soles.*

sedimentation rate was 31 mm. per hour (Wintrobe method). The blood nonprotein nitrogen was 34 mg., and the total serum protein 7.0 gm. per 100 cc., with 3.8 gm. of albumin and 3.2 gm. of globulin. The icteric index was 6, and the thymol turbidity 8.4 units. A culture of the bullous fluid was sterile.

The patient was treated with intramuscular aqueous penicillin and boric acid soaks and ointment locally, saline mouth washes; 10 per cent zinc sulfate solution was instilled in the eyes three times daily. He made a gradual and uneventful recovery, the skin lesions healing without scarring in about 3 weeks and the urine returning to normal.

After he had recovered clinically, he was tested for sulfonamide sensitivity. First, a patch test, consisting of a pulverized sulfathiazole tablet made into a paste by mixture with a small amount of distilled water, was administered to the unbroken skin. The results were negative, and 2 days later, the passive transfer test, after the method described by Leftwich,[13] was performed by the intradermal injection of 0.05 cc. of serum from another patient, who had a sulfadiazine blood level of 7.0 mg. per 100 cc. and whose serologic test was negative. There was no reaction, either local or systemic, and the next day the patient was discharged from the hospital. On the day of discharge his face and scalp began to itch, and 3 days later bullae began to appear on his thighs and forearms and then on his eyelids and in his mouth and finally on the rest of his body. He stated that he had taken no medication of any kind

FIGURE 3. *Balanitis and Denuded Areas on the Penis and Scrotum.*

since discharge and knew of no contact that could have caused the eruption. On readmission, 1 week after his discharge, his appearance, physical findings and laboratory data were almost identical to those of the previous admission. The same course of treatment was pursued, and again, in approximately 3 weeks, the lesions had healed. Since the relation between the passive transfer intradermal test for sulfadiazine and the eruption, which started 2 days later, was not recognized, he was given a test dose of 0.5 gm. of sulfadiazine orally. Within 2 hours he began to have a generalized pruritus, and 3 hours later the temperature rose to 101°F., and he had a shaking chill. Subsequently, he became comfortable and slept for 3 hours, after which he awoke nauseated and vomited, intermittently, for 2 hours and, while walking to the lavatory, became giddy and fell to the floor. At this time the respiration became fast and labored, at a rate of 30 per minutes; the pulse was 110 and weak, and the blood pressure was 100/60. He was given 100 mg. of pyribenzamine orally four times daily. About 12 hours later he complained of a "skim" over his eyes, and conjunctival injection was noted. At this time, one of the darkly pigmented areas that marked the sites of the bullae of the previous eruption had formed a new bulla. A purulent urethral discharge was also noted, which yielded *Staphylococcus albus* on culture. The temperature rose to 104°F. By the next morning, his skin, mucous membranes and conjunctivas were involved as before, and identical treatment was instituted. Because of the large amount of serum that continued to ooze from the denuded areas, the patient was given transfusions of 500 and 1000 cc. of whole blood on the 3rd and 4th days of the eruption, respectively, and a pressure dressing over petrolatum-impregnated gauze was applied to the extremities; furacin ointment was applied to the trunk and buttocks because of the development of suppuration. Two weeks after the administration of the oral sulfadiazine, the temperature gradually subsided to normal. The mucous membranes had healed, and conjunctivitis disappeared; in 3 more days, the remaining skin lesions had again healed without scarring.

Discussion

Although the patient was able to give no past history of exposure to sulfonamide, the onset of fever followed by the eruption and conjunctivitis, which occurred on the second day (rather than after seven or ten days) of sulfonamide therapy in December, 1947, suggested previous sensitization to the drug. In retrospect, it might be conjectured that the "erythema multiforme" reported from 1945 followed the use of the drug at that time.

There are numerous reports in the literature of cases in which very small doses of a sulfonamide caused severe, generalized skin reactions.[7, 14] Cohen, Thomas and Kalisch[14] reported the appearance of a generalized pruritic rash six hours after the local application of 8 mg. of sulfathiazole powder, the patient having developed a skin rash two weeks previously, after the use of sulfathiazole ointment locally. Farrington and Wolff[15] described the reproduction of a generalized, oozing, vesicular eruption by simultaneous patch testing with sulfanilamide and sulfathiazole a month after the original eruption, which had been caused by the local use of sulfanilamide. They also described "an intense necrotizing reaction of the buccal mucosa upon application of approximately 8 mg. of sulfathiazole to the mouth of a previously sensitized patient" after the method described by Goldman and Goldman.[16] The patient discussed above, on the other hand, showed neither a local nor systemic reaction after application of a patch test of sulfathiazole, although the eruption that appeared in December, 1947, was apparently due to the oral administration of that drug.

Although Leftwich[13] performed 300 intradermal tests for sulfonamide sensitivity, he reported no generalized reactions, and of 30 sensitive patients, 28 had positive tests, the reactions appearing immediately and fading within thirty minutes to an hour and a half. In contrast to these results, the patient in the case reported above showed no immediate or local reaction, but responded to the test by a delayed (twenty-four to forty-eight hours) generalized, severe reaction.

The experience of Farrington and Wolff with the patch test, the reaction with the intradermal passive transfer test and the patch test and the oral test dose discussed above, as well as the reports of others describing severe reactions from small doses of the drug, administered both locally and systemically, have illustrated the potential danger and unreliability of testing for sulfonamide sensitivity. It should be emphasized also that despite reports in the literature describing the treatment of erythema multiforme by sulfonamides, this form of therapy should be used with caution unless one is absolutely certain that the syndrome was not caused itself by use of the drug.[17-20] This, of course, is true because of the difficulty in clinical differentiation of the bullous eruption sometimes seen in sulfonamide toxicity from idiopathic erythema multiforme.

Summary

The bullous eruptions that may result from sulfonamide toxicity are often clinically indistinguishable from idiopathic erythema multiforme exudativum. To establish the role of the sulfonamides in an obscure case, several tests for sulfonamide hypersensitivity are available.

A case illustrating the unreliability of the patch test, an untoward and at first unrecognized reaction to the intradermal passive transfer test and a severe reaction following an oral test dose of sulfonamide is reported. It is believed, therefore, that testing for sulfonamide sensitivity should be approached with care, as should the treatment of erythema multiforme exudativum with sulfonamide, as recommended by some, unless it is certain that this drug is not the etiologic agent.

References

1. Hebra, F. *Diseases of the Skin.* Vol. 1. Translated and edited by C. H. Fagge. London: New Syndenham Society, 1866.
2. Keil, H. Erythema multiforme exsudativum (Hebra): clinical entity associated with systemic features. *Ann. Int. Med.* **14**:449-494, 1940.
3. Bailey, J. H. Lesions of cornea and conjunctiva in erythema exudativum multiforme (Hebra): report of three cases with grave ocular sequelae. *Arch. Ophth.* **6**:362-379, 1931.
4. Fletcher, M. W. C., and Harris, R. C. Erythema exudativum multiforme (Hebra) — bullous type: cases seen in contagious disease hospital. *J. Pediat.* **27**:465-479, 1945.
5. Dardinski, V. J. Erythema multiforme bullosum following use of sulfadiazine. *Am. J. Clin. Path.* **15**:28, 1945.
6. Greenberg, S. I., and Messer, A. L. Fatal bullous dermatitis following administration of sulfadiazine. *J. A. M. A.* **122**:944, 1943.
7. Livingston, C. S., and Pillsbury, D. M. Sulfathiazole in eczematous pyoderma: sensitization reaction to successive local and oral therapy: report of 12 cases. *J. A. M. A.* **121**:406-408, 1943.
8. Robitzek, E. H. Fatal pemphigoid reaction to diasone. *Am. Rev. Tuberc.* **51**:473-477, 1945.
9. Raffetto, J. F., and Nichols, S. Nearly fatal reaction to sulfadiazine in ten-year-old girl involving skin, eyes, and oropharynx. *J. Pediat.* **20**:753-755, 1942.
10. Ellis, F. A. Reactions to nirvanol, phenytoin sodium and phenobarbital: report of case of ectodermosis erosiva pluriorificialis following ingestion of phenytoin sodium. *South. M. J.* **36**:575-579, 1943.
11. Ritchie, E. B., and Kolb, W. Reaction to sodium diphenyl hydantoinate (dilantin sodium): hemorrhagic erythema multiforme terminating fatally. *Arch. Dermat. & Syph.* **46**:856-859, 1942.
12. Newman, B. A. Phenolphthalein intoxication. *J. A. M. A.* **101**: 761-764, 1933.
13. Leftwich, W. B. Intradermal test for recognition of hypersensitivity to sulfonamide drugs. *Bull. Johns Hopkins Hosp.* **74**:26-48, 1944.
14. Cohen, M. H., Thomas, H. B., and Kalisch, A. C. Hypersensitivity produced by topical application of sulfathiazole. *J. A. M. A.* **121**: 408-411, 1943.
15. Farrington, J., and Wolff, B. P. Exfoliative dermatitis caused by sulfonamides and its reproduction by patch testing. *North Carolina M. J.* **7**:555, 1946.
16. Goldman, L., and Goldman, B. Contact testing of buccal mucous membrane for stomatitis venenata. *Arch. Dermat. & Syph.* **50**: 79-84, 1944.
17. Kove, S. Stevens-Johnson syndrome (eruptive fever with stomatitis and conjunctivitis). *Am. J. M. Sc.* **210**:611-623, 1945.
18. Bregman, A. Treatment of erythema multiforme exsudativum with sulfanilamide. *Arch. Dermat. & Syph.* **38**:623, 1938.
19. Fitzgerald, P. J. Fatal bullous dermatitis with multiple lesions of mucous membranes: therapeutic failure of sulfadiazine and penicillin. *U. S. Nav. M. Bull.* **47**:134-141, 1947.
20. Wright, D. O., Gold, E. M., and Jennings, C. Stevens-Johnson syndrome: report of nine patients treated with sulfonamide drugs or penicillin. *Arch. Int. Med.* **79**:510-517, 1947.

FERTILITY STUDIES IN THE HUMAN MALE WITH TRAUMATIC INJURIES OF THE SPINAL CORD AND CAUDA EQUINA*

HERBERT W. HORNE, M.D.,† CAPTAIN DAVID P. PAULL, MC, AUS,‡ AND DONALD MUNRO, M.D.§
BOSTON AND FRAMINGHAM, MASSACHUSETTS

HUMAN males who have suffered traumatic injuries of the spinal cord and cauda equina have long been considered sterile. This study was performed to determine whether or not this assumption is true. A previous paper[1] discussed the incidence of erection and ejaculation in the human male with traumatic injuries of the spinal cord and cauda equina.

The 18 cases studied in the present series were patients at Cushing Veterans Administration Hospital who had suffered traumatic injuries of the spinal cord and cauda equina. Their ages ranged from twenty-one to thirty-five years, with an average age of twenty-seven years. The length of time that had elapsed since the original spinal-cord or cauda-equina injury ranged from nine to seventy-two months, with an average of forty-seven months. No effort was made to select the cases to be studied, and the only requirements on the part of the patient were that he show consistent interest in the project, that he be voiding without a catheter and that he be in good general physical condition. Many other patients were anxious to be included in the investigation, but time did not permit a larger series.

For the purpose of this paper, the patients are classified as to the level of injury and as to the type of injury. The levels of injury of the spinal cord are reported as dermatome segments. Injuries of the cauda equina are classified separately.

The types of injury are classified in the same manner as that used in the first paper of this series[1]:

> Patients diagnosed as suffering from a transection have been divided into two groups, depending upon the accuracy of verification of the diagnosis. In those diagnosed as Anatomic-Visualized Transection (Tr.-A) the injury has been actually seen at laminectomy to be one in which there is a complete separation of the cut ends of the cord. In those diagnosed Clinical-Not Visualized Transection (Tr.-C) either the cord injury has not been seen or, if seen, the continuity of the cord was found to be either grossly intact or maintained by intervening scar tissue. The character and length of the clinical course taken by the patient, however, have justified the diagnosis of transection. In both instances, only patients with a complete sensory and voluntary motor loss of function below the level of the cord injury are included as cord transections. Patients diagnosed as suffering from a Partial Cord Injury (P) are those in whom it has been possible to demonstrate some degree of retention of either sensation or voluntary motion, or both, in the body and extremities below the level of maximal cord injury. The same diagnostic criteria have been applied to patients with cauda equina (C.E.) injuries.

Clinical investigation of these cases included, in addition to routine procedures, evaluation of the external and internal genital organs and the neurologic status. There were no gross changes in the external genitalia except for the cases in which an attack of epididymitis had occurred. In these cases there was invariably a persistent residual induration of the involved epididymis. One patient (Case 7) had a unilateral testicular atrophy secondary to mumps in childhood, and another (Case 1) had a unilateral cryptorchid testis. Virtually all the prostate glands were small, flat, nonnodular and soft.

Semen samples were obtained by electrical stimulation in all cases except 3 (Cases 1, 5 and 18), in which masturbation produced the specimen. A McIntosh No. 5005 portable-wall-plate physiotherapy machine was used to supply the stimulus. This machine delivers predetermined variable amounts of current across a 90-volt potential. The inactive electrode was soaked in tap water and placed under the patient's sacrum with the patient lying on his back. The active electrode was a No. 28 curved urethral sound. This sound was covered with rubber tubing except for the handle and the terminal 5 cm. Electrical stimulation was accomplished by applying sinusoidal and faradic current of 45 and 60 milliamperes, respectively, to the active electrode, which had been introduced into the rectum. The bare tip of the sound was applied successively to the region of each seminal vesicle and the prostate, this sequence being carried out first with sinusoidal, then faradic and, finally, sinusoidal current again. The duration of stimulation in each position was approximately 4 seconds. After withdrawal of the active electrode, digital massage successively of the seminal vesicles and the prostate was performed. The semen was then milked from the urethra. No complications, local or otherwise, have followed over 100 treatments of this sort. Massage of the seminal vesicles and prostate without prior electrical stimulation produced fluid devoid of spermatozoa in all but 1 case, when a few spermatozoa were found on one occasion. Electrical stimulation followed by massage produced semen specimens as shown in Table 1. We are frank to state that how or why the electrical stimulation is effective is not clear. Suffice it to say that

*From the Surgical and Paraplegia Services, Cushing Veterans Administration Hospital, Framingham, Massachusetts.

Presented at the annual meeting of the New England Surgical Society, New Haven, Connecticut, October 2, 1948.
Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the authors.

†Assistant resident, Free Hospital for Women; formerly, resident in surgery, Cushing Veterans Administration Hospital.
‡Resident in surgery, Cushing Veterans Administration Hospital.
§Assistant professor of neurosurgery, Harvard Medical School; associate professor of neurosurgery, Boston University School of Medicine; chief, Department of Neurosurgery, Boston City Hospital.

with electrical stimulation, followed by massage, semen specimens containing spermatozoa have been consistently obtained in 11 of the 18 cases in which simple massage had failed. In each case the first few examinations were not productive of spermatozoa, whereas subsequent trials usually were successful.

Semen analysis was carried out by the technic of Williams and Simmons.[2] In all except Case 5, in Case 1 has a partial cervical injury and is able to have erections, ejaculations and intercourse in an approximately normal manner. The patient in Case 5 is of particular interest because he has a clinically complete transection of the spinal cord at the sixth thoracic segment. This case was reported in detail in the previous paper.[1] On March 6, 1948, this patient was left alone in a room and asked to obtain a semen specimen. He shortly

TABLE 1. *Data in Patients with Injuries to the Spinal Cord and Cauda Equina.*

Case No.	Level of Injury	Type of Injury	Blood Count	Basal Metabolic Rate	Testicular Disease and Epididymitis	Testicular Biopsy	Total Motile Spermatozoa Count	Erections	Ejaculations	Coitus	Pregnancy
				%							
1	C5	Partial cord injury	Normal	−10	Cryptorchid, unilateral	—	30,000,000	Yes	Yes	Yes	Yes
2	T3	Clinical-not visualized transection	Normal	0	Epididymitis, unilateral	—	48,000,000	Yes	No	Not tried	—
3	T4	Clinical-not visualized transection	Normal	—	—	—	500,000	Yes	No	No	—
4	T6	Anatomic-visualized transection	Normal	−2	—	—	0	No	No	No	—
5	T6	Clinical-not visualized transection	Normal	−10	—	—	110,000,000	Yes	Yes	Yes	Yes
6	T6	Clinical-not visualized transection	Normal	−25	—	—	3,000,000	No	No	No	—
7	T6	Partial cord injury	Normal	+3	Post-mumps atrophy, unilateral	—	3,000,000	Yes	No	No	—
8	T8	Anatomic-visualized transection	Normal	−13	—	Spermatogenic arrest	600,000	Yes	No	No	—
9	T11	Clinical-not visualized transection	Normal	−13	—	Practically no spermatogenic cells; occasional active tubule.	500,000 (nonmotile)	No	No	No	—
10	T11	Partial cord injury	Normal	—	—	—	None	Yes	No	No	—
11	T12	Partial cord injury	Slight anemia	—	Unilateral epididymitis	—	None	Yes	No	Yes	—
12	T12	Partial cord injury	Slight anemia	−9	—	Normal	75,000,000 (nonmotile)	No	No	No	—
13	L1	Clinical-not visualized transection	Normal	—	Recurrent, bilateral, severe epididymitis	Left, atrophy; right, normal.	None	No	No	No	—
14	L1	Clinical-not visualized transection	Normal	+2	—	Normal	30,000,000	Yes	No	Yes	—
15	L1	Partial cord injury	Slight anemia	−4	—	Maturation arrest of germinal epithelium	None	No	No	No	—
16	Cauda equina	Clinical-not visualized transection	Normal	+5	—	Tubular atrophy; Leydig hyperplasia without germ cells.	Rare, nonmotile	No	No	No	—
17	Cauda equina	Partial injury	Normal	+13	Unilateral epididymitis	—	None	Yes	No	No	—
18	Cauda equina	Partial injury	Normal	—	Unilateral epididymitis	—	80,000,000	Yes	Yes	Yes	—

semen analyses were carried out on each patient a minimum of three times. The figures stated in Table 1 represent the highest values obtained in each case. Case 5 had one examination only. The chemical determinations, the blood counts and the determinations of basal metabolic rates were done in the hospital laboratory. Reports on seven testicular biopsies were made by the hospital pathologist, Dr. Robert Fienberg, and reviewed by Dr. Fred Simmons.

The wives of the patients in Case 1 and 5 have become pregnant since these patients have returned home from the hospital. The patient presented a specimen, the analysis of which was as follows:

Amount	Turbidity	Sperm atozoa Count	Motility	Differential	
cc.		*million/cc.*	*26%*		
4	++++	115	+ to ++++	Normal	75
				Pyri	17
				AA	5
				Macro	0
				Micro	3
				Misc	0

Discussion

In this study there seems to be no striking correlation between the level or type of injury and the

total sperm counts. Patients with injuries to the cauda equina and lumbosacral cord have lower counts in this series, but it is believed that there are not a sufficient number of cases for definite conclusions to be drawn. It is interesting that the patient in Case 13, who had a clinical-not visualized transection at the first lumbar segment, had a normal right testicle by biopsy. This particular patient has had repeated attacks of epididymitis bilaterally, which may well explain the absence of spermatozoa in the semen specimen.

Basal metabolic rates fell, for the most part, within the lower limits of normal. Testicular biopsies in 7 cases varied from complete atrophy of spermatogenic cells to normal testicular activity. The correlation of the spermatozoa counts and the testicular biopsies is reasonably close except in Case 13. The reason for this one aberration is discussed above.

Conclusions

Traumatic injury of the spinal cord does not in itself preclude fertility.

A technic is described for obtaining semen specimens from patients having spinal-cord injuries who are unable to ejaculate.

A patient with a clinical-not visualized transection at the fifth thoracic dermatome is capable of erection and ejaculation of normal semen and has successfully impregnated his wife.

We are indebted to Dr. Fred A. Simmons and Dr. George P. Denny for their assistance respectively in the sterility and medical aspects of this study.

References

1. Munro, D., Horne, H. W., Jr., and Paull, D. P. Effect of injury to spinal cord and cauda equina on sexual potency of men. *New Eng. J. Med.* **239**:903-911, 1948.
2. Williams, W. W., and Simmons, F. A. Clinical approach to diagnosis of sterility. *Urol. & Cutan. Rev.* **47**:558-570, 1942.

MEDICAL PROGRESS

THORACIC SURGERY (Concluded)

J. Gordon Scannell, M.D.*

BOSTON

Results of Treatment

It is difficult to assess the problem of cancer of the lung in relation to the population as a whole on the basis of reported hospital series. However, it is apparent that in the course of the past ten years, the operability and resectability rates of cancer, as seen by the surgeon, have increased. Björk[70] has reported at length the clinical experience with bronchogenic carcinoma at the Brompton and Royal Cancer hospitals. Of 996 cases in which the clinical diagnosis was made (combining the material of both medical and surgical services from 1937–1944), 15.3 per cent were adjudged suitable for thoracotomy, and 7.5 per cent (or 49 per cent of those explored) were resectable. However, annual operability and resectability rates increased from 8.2 per cent and 5.1 per cent of 134 total cases seen in 1937 to 25.6 per cent and 13.5 per cent, respectively, of 133 cases in 1944. Ochsner, DeBakey and Dixon[71] report that of 360 cases seen on a *surgical* service between 1936 and 1946, 251 (70 per cent) were considered operable, 210 (58 per cent) were actually explored, and 129 (36 per cent) were resectable. In reviewing the Johns Hopkins series of 327 cases of carcinoma of the lung "referred for surgical treatment" and presumably explored, Rienhoff[72] reports that 34 per cent were resectable. Thus, of 1950 cases in nine surgical reports since 1940, 782 (40 per cent) were operable, and 432 (22 per cent) were resected.[62] By and large, however, these reports represented total experience with the disease and therefore do not reflect changing trends over the years. The importance of defining the material studied in terms of microscopical rather than clinical diagnosis has long since been amply demonstrated (Churchill, 1940). Furthermore, the tremendous number of variables, not always apparent in the random selection of clinical material, must be kept in mind.

During the period of increasing limits of operability and of technical standardization, statistics of operative mortality have required almost annual revision downward. The figures of a mere ten years ago are currently of historical interest chiefly. Of more significance as a basis for evaluating present-day surgical therapy are such figures as those of Jones[73] — 52 consecutive pneumonectomies, 1942–1946, with 2 deaths (based on a resectability rate of approximately 20 per cent of cases seen) — and of Adams[74] — an operative mortality of 5.1 per cent in 39 resections for carcinoma, 1942–1947 (resectability rate of approximately 30 per cent of cases seen).

*Instructor in surgery, Harvard Medical School; assistant in surgery, Massachusetts General Hospital.

A correct appraisal of operative risks is obviously important in a decision for pneumonectomy versus lobectomy in carcinoma of the lung. Majority opinion at present favors total pneumonectomy with as extensive a lymph-node dissection as possible, to include the subcarinal nodes, the azygos node on the right and the nodes in the pulmonary ligament. If one chooses to argue by analogy to carcinoma of the breast, the position is a strong one, and certainly, other things being equal, total extirpation of a cancer-bearing organ with regional-lymph-node dissection en bloc is a major desideratum of cancer surgery. However, if one argues by analogy to gastric carcinoma, in which mortality, morbidity and disability of total versus subtotal gastrectomy are not equal, the question of lobectomy for cancer of the lung must be kept open.

Granted that it may be more informative to consider that Graham's patient, in whom a total pneumonectomy was done in 1933 for squamous-cell carcinoma of the lung, is still alive and well than to consider survival statistics at present on record, a preliminary estimate of efficacy of resection, when it is possible, may be made from the reported experience of Adams[74] (1948), Rienhoff[72] (1947), Ochsner et al.[71] (1947) and Graham[75] (1948). In so doing, one finds a total of 133 cases of pneumonectomy done five or more years prior to publication. Of these, 36 patients, or 27.1 per cent, survived five years. One of the greatest variables in the material has been the extent of the disease at the time of operation, for, as Ochsner and his associates have reported, if the disease extended beyond the lung — that is, encroachment on contiguous structures or metastasis to regional lymph nodes — only 2 of 27 patients survived three years, and none beyond six years. Yet of 15 of Graham's 53 patients who survived pneumonectomies beyond five years, 6 had positive lymph nodes at the time of operation. Coleman[76] has recently made the interesting observation that of 88 histologically proved cancers of the lung in his series, 6 that invaded ribs were all of squamous-cell origin (as opposed to 47 per cent of the entire series). Resection could be carried out in 5 of these patients, of whom 1 was alive and well six years and 1 two years after operation. Resection of portions of the chest wall had been carried out in 6 of Ochsner's series.

By way of contrast it would be desirable to present survival statistics for a comparable series of lobectomies done with a "curative" rather than a "palliative" objective. Unfortunately, such statistics are not presently available. In 1947 Adams[77] reported 5 cases of lobectomy for carcinoma with five-year survivals in 3, and Neuhof and Aufses[78] 24 cases with two-year survivals in 7. The latter authors have urged the importance of reporting results on the basis of the topographic features of the patient's disease, and have advocated pneumonectomy in the carcinomas of main and branch bronchus — usually infiltrative with diffuse lymph-node involvement — and lobectomy for the circumscribed cancers without lymph-node spread and peripherally invasive carcinomas. They have stated, and this opinion was shared by few, that microscopical features were of relatively little significance after radical excision. Needless to say, survival statistics of two years in carcinoma must be accepted with caution.

Graham[75] has agreed that lobectomy may have a place in the treatment of carcinoma of the lung, but that if the mortality and morbidity of pneumonectomy can be kept low, the latter is the procedure of choice. As noted above, in 15 of his series of 53 pneumonectomies done prior to 1942, the patients were living and well in 1947. Head[79] has argued that in the older age group, pneumonectomy is a "crippling" operation, and that he has preferred lobectomy in this group when feasible. He has also warned against pneumonectomy under a mistaken diagnosis of cancer, believing that lobectomy is often indicated as a relatively safe excision biopsy when the diagnosis is in doubt. Janes[80] has recently reported 2 instructive cases of lipoid pneumonia simulating bronchogenic carcinoma treated surgically. Adams has suggested the following three broad indications for consideration of lobectomy: peripheral lesions of the lower lobes without grossly involved lymph nodes; upper-lobe lesions in which a clean dissection of the lobar bronchus is possible; and "palliation." Consideration of the anatomy of the tracheobronchial lymphatics[81] serves to emphasize the relatively small increment of lymph-bearing tissue removable by pneumonectomy over lobectomy in many lesions, particularly of the upper lobe.

Birath, Grafoord and Rudström[82] have recently discussed the quantitative measurement of pulmonary function after lobectomy and pneumonectomy. Their point of departure was the well known and previously studied[83] distention of the remaining lung following pneumonectomy. Total lung volume and its fractions were measured by external spirometry with a closed-circuit system, and respiratory dead space estimated by construction of a washing-out curve of nitrogen from the lungs. The latter principle has been explored extensively by Cournand and others, and has recently been elaborately refined by Bateman[84] at the Mayo Clinic. The material of Birath et al.[82] included 12 cases of pneumonectomy and 14 of lobectomy, all in adults, two to thirteen years after operation. As one might expect, after pneumonectomy the volume of the remaining lung was found to exceed by about 15 per cent the calculated normal values, the functional residual air was approximately 50 per cent higher than the predicted value for a normal lung, and the absolute residual air was even greater than 50 per cent. Thus, within the limits of the method, particularly regarding prediction of nor-

mals, the cases resembled emphysema. The cases of lobectomy showed a similar but less marked deviation from the predicted levels. Maximum breathing capacity, breathing reserve and rate of oxygen utilization were not reported. Of possibly greater significance than the actual laboratory measurements were the estimates of working capacity and dyspnea after the two procedures. In the 12 cases in which pneumonectomies were performed, 9 patients had full working capacity, 2 were unable to work, and 1 was limited to half capacity. All 14 of the patients with lobectomies were reported to have full working capacity. Rienhoff[72] has reported that all his patients except 1 (a professional boxer) who lived any significant time after pneumonectomy for cancer were restored to normal activity. Quantitative measure of rehabilitation of the patient after pneumonectomy is obviously difficult, but some estimate is essential in the planning of the surgical program for the patient.

When one evaluates the efficacy of surgical treatment, it is only fair to contrast it to alternative forms of therapy or no therapy at all. From the point of view of survival, the evidence appears to be clear. Untreated, survival beyond one year of the onset of symptoms or establishment of the diagnosis is rare. Radiation therapy holds some promise of palliation over and above the rigors of treatment, and appears to prolong survival beyond predicted limits. Widmann[85] has contrasted 167 patients with microscopically proved cases that were treated against 119 not treated. Of the latter, none lived a year. Of the 167 patients treated, 18 lived over one year, 2 for two years, 1 for three years and 1 for 5 years, and 1 was free of clinical evidence of disease six years after treatment. However, on the other side of the ledger, 89 per cent of the patients treated lived less than a year. Leddy and Moersch,[86] in 1940, compared 125 radiation-treated cases to a control series of 125 untreated. Clinical characterization of the two groups was remarkably similar. A salient fact of their study was that no untreated patient survived more than one year, whereas after treatment 25 patients lived one or more years, and 5 for five years or more, with 1 fourteen-year and 2 ten-year survivals in the latter group. All cases were proved histologically. Beyond improving survival time, the procedure was considered worth while on the evidence for palliation of pain and cough. Shorvon[87] has recently reported 111 cases treated by "radical" x-ray therapy. No patients survived beyond three years. Hocker and Guttman,[88] at the Memorial Hospital, discussed as a preliminary report 93 patients receiving million-volt therapy. At the time of publication in 1944, 21 patients were surviving, 4 for more than two years, and but 2 of these had no clinical evidence of disease.

Metastatic Tumors of the Lung

Alexander and Haight[89] have recently collected 24 cases in which pulmonary resection has been carried out for presumably solitary metastatic carcinoma or sarcoma. Six of these cases were from their own clinic, and the remainder were collected from the literature or by personal communication. Twelve patients had no recurrence, 8 of them sufficiently long (twelve, seven, six, five, four, three, one and a quarter and one year) after operation to justify optimism. In this series, the patients with sarcoma appeared to do better than those with carcinoma. Six of the cases were done for renal-cell carcinoma, including 1 case in which the patient has survived for thirteen years after pulmonary resection of a metastatic hypernephroma.

Effler and Blades[90] have recently added 3 cases, including 1 patient who, nine months after resection of a pulmonary metastasis from a sigmoid carcinoma, resected two years previously, had a cerebral metastasis removed. A recent case at the Massachusetts General Hospital demonstrates the vagaries of metastatic disease. The patient, a seventy-two-year-old man, underwent a removal of the right upper lobe for malignant melanoma metastatic to the lung. Fifteen years before, he had had an enucleation of the left eye for a similar tumor.

Tuberculosis

In his progress report for 1944, Strieder[91] pointed out that only recently had accepted technics been generally applied to excisional surgery for pulmonary tuberculosis. Useful as tourniquet lobectomy had been, results in the treatment of tuberculosis had been most disappointing and marred by innumerable difficulties with the bronchial stump and spread of disease during a complicated convalescence from surgery. With the proved value of individual ligation technic, the incidence of these hazards was reduced, and the question of lobectomy reopened with new enthusiasm.

By 1944, a sizable number of cases of lobectomy, with relatively few complications directly chargeable to the operative technic, had been compiled. Strieder has reviewed these at length, and pointed out the need of more time before any proper evaluation of the results can be made.

At present the long-term results of lobectomy for tuberculosis still await definition, and a new technical consideration — namely, the use of streptomycin — has entered the picture. Streptomycin therapy for tuberculosis has had extensive and critical trial in the facilities of the Veterans Administration. A report of its Streptomycin Committee[92] demonstrates that the practice of combining surgical procedures with streptomycin is of proved value. Beginning in March, 1947, a study

was carried out in 27 hospitals in which the drug was given arbitrarily for seven days preoperatively and fourteen days postoperatively, to alternate thoracoplasty patients. Daily dosage varied between 1.0 and 2.0 gm. Streptomycin was also given to the great majority of other patients undergoing extensive surgical procedures for tuberculosis. In all, 1559 operations were performed upon 709 patients, of whom 406 received streptomycin. In the thoracoplasty group, the difference of spreads between treated (2.0 per cent), and untreated (5.6 per cent) was statistically significant, but in spite of this, the *routine* use of streptomycin was not advocated in thoracoplasty patients, not only because the relatively low incidence of spread in untreated cases made the practice somewhat wasteful of a rather expensive agent, but also because of toxic implications and a definite hazard of producing bacteriologic resistance. An incidence of only 4 postoperative spreads following 144 pneumonectomies and lobectomies was regarded as ample demonstration of the value of streptomycin in these procedures, in which its routine use was recommended. A total of 1.0 gm. daily, divided into two doses and administered intramuscularly, appeared to be effective and was relatively innocuous.

The subject was accorded considerable recognition at the 1948 meeting of the American Association for Thoracic Surgery. Noteworthy was the increasing enthusiasm shown for pulmonary resection, and the reporting of rather large series of cases in which major surgical procedures could be carried out under the "benevolent mantle" of streptomycin. O'Brien et al.[93] rejoiced that now the maximum of definitive surgery for pulmonary tuberculosis was possible with a minimum of preliminary procedures. Active cases required a less prolonged cooling-off period than formerly before a surgical program was undertaken. In terms of operative morbidity and mortality, and also of early conversion of sputum to normal, it was apparent that immediate results were improved by use of the agent.

In 1946 Sweet[94] reported the total experience with pulmonary resection for tuberculosis at the Massachusetts General Hospital in the period before streptomycin was employed. The material consisted of 27 lobectomies, including the 6 reported by Churchill and Klopstock[95] in 1943, and 36 pneumonectomies. The surgical problems of the two groups were kept clearly distinct.

Of great interest were the 11 lobectomies that were done as alternative to thoracoplasty. The other 16 were done for the more generally acceptable indications: location of cavity unfavorable for collapse therapy; tuberculoma; atelectasis distal to stenosis; and large, rigid-walled cavity. In many of the cases adjudged suitable for lobectomy, it was striking to discover how much disease not clearly visualized by x-ray examination existed in other portions of the lung. One, therefore, could speak with propriety of reactivation rather than of spread. Among the 27 lobectomies there were 2 postoperative deaths, 5 patients died later of their disease, 7 were alive with their disease (with positive sputum), and 13 were apparently well one to three years after operation. Among the 13 apparently well patients were 7 of the 11 patients in whom ordinarily a thoracoplasty would have been done in anticipation of a good result. Four of the 11 "alternative to thoracoplasty" patients were alive with disease at the time of the report. Of the 2 lobectomy cases that showed early reactivation of the disease, 1 was fatal, and the other cleared. Of 11 patients who suffered "late" reactivation of the disease, 4 were dead, and the remainder ill at the time of the report.

Of the 36 pneumonectomy cases, 18 were considered "desperate risks" with an excavated and almost functionless lung, and all with obviously bilateral disease on x-ray study. Of the other 18, stenosis of the main bronchus accounted for 6, and persistent cavity under properly performed thoracoplasty for 4 cases. In 5 the choice of pneumonectomy was made at operation when incomplete or absent fissures made transection of tuberculous disease almost inevitable. Seven of the patients with pneumonectomies (19.4 per cent) died in the early postoperative period; 7 died later of their disease; 5 were alive with disease, and 17 were apparently well. Among the latter were 3 of the 18 with "destroyed lungs," 5 of the 6 with "bronchostenosis," 4 of the 5 in whom the operation was done for technical reasons, and 3 of the 4 in whom thoracoplasty was a failure. The salvage of only 3 of 18 patients regarded as desperate risks, with 4 early and 6 late deaths in this group, was disappointing, and emphasized the importance of the patient's response to his disease as predetermining the success of radical surgery. In the other patients who handled their disease well biologically, radical surgery as a mechanical corrective measure appeared to be quite effective.

Overholt[96] has also reported his extensive pre-streptomycin experience with resection for pulmonary tuberculosis — 192 cases done between 1934 and 1946 — and has advocated certain technical points. Of these the face-down position has been much debated. According to its proponents, its advantages lie in less gravity drainage to the sound lung, less impairment of the chest wall and diaphragm on the sound side, less mediastinal shift, elimination of the necessity of positive pressure and the direct approach to the hilus posteriorly, with less need for hilar traction. In reply, others have advanced cogent reasons for employing the posterolateral and the anterior approach according to individual indications and preferences of both the operator and the anesthetist. Overholt has ad-

vocated routine postresection thoracoplasty in an effort to control excessive expansion of the remaining lung. In 1944, Chamberlain[91] stressed the factor of overdistention as a real consideration in the choice of selective thoracoplasty over upper lobectomy. His argument was supported by bronchospirometric studies. Maier,[91] after similar studies, challenged this position. Of Overholt's patients, only 16 per cent with upper lobectomies done as alternative to thoracoplasty had ipsilateral exacerbations if post-lobectomy thoracoplasty (second, third and fourth ribs) were done, whereas the exacerbations appeared in 50 per cent who had no postoperative collapse therapy. It seems important, therefore, to demonstrate the superiority of lobectomy and thoracoplasty over thoracoplasty alone — a demonstration still forthcoming.

The heterogeneous field of extirpation for pulmonary tuberculosis has been extended to include segmental resection in a certain number of cases. The physiologic considerations of conserving lung tissue, for both its respiratory and its space-filling functions, seems to be secondary to pathologic considerations regarding the segmental nature of the disease in any given case. Reluctance to transect tuberculous tissue has been a well established principle, although streptomycin may alter this established conviction, and increasing familiarity with technics of segmental resection add some degree of safety. The fundamental nature of the disease and the objectives of surgical treatment must, however, remain the most important considerations.

Coccidioidomycosis

Coccidioidomycosis, heretofore considered rare but disabling and often fatal, has achieved rather widespread clinical significance as a result of infection and dissemination of the disease among members of the armed forces. Its pathogenesis and pathology have been authoritatively reviewed by Forbus and Bestebreurtje.[97] Ninety-five cases of the disseminated form of the disease occurring in the armed forces between 1941 and 1946 are reported; 50 of these were studied clinically and at autopsy, the other 45 were confirmed by biopsy. It was apparent that coccidioidomycosis is primarily a pulmonary disease and rarely fatal except in association with endogenous reinfection. Pathologically, it is a "granulomatous" process, with many characteristics of tuberculosis, and also of many of the ordinary pyogenic infections. Primary pulmonary coccidioidomycosis is usually represented by a focal or diffuse nongranulomatous inflammatory response with regional lymphadenitis. In its severe forms, genuine suppurative and granulomatous lesions, which are sometimes destructive enough to go on to cavity formation, develop. The severe forms, which are rare, heal by scar formation, and these lesions may become calcified. Secondary or disseminated disease often develops during the active progress of the primary infection, or may spring from vegetative organisms smouldering in clinically healed but residual lesions. The authors collected 5 cases in which operation was performed when neoplasm was suspected on x-ray examination and could not be excluded. It is believed that, for approximately ten years, disseminated endogenous reinfection will continue to occur among members of the armed forces who were trained in endemic areas of the Southwest, but it does not appear likely that the disease will spread to nonendemic areas.

Greer, Forsee and Mahon[98] have reported 15 surgically treated patients from Fitzsimons General Hospital, in whom focal pulmonary coccidioidomycotic lesions were present. These appeared as either solitary or cavitary circumscribed lesions, which closely simulated tuberculosis and from which positive pathological differentiation was possible only by recognition of the organism in tissue sections or by isolation in cultures of the lesion. Nine were treated by lobectomy, and 6 by wedge excision. In the presence of cavitation, the presence of daughter granulomas made lobectomy the preferable procedure. The indications for operation included recurrent hemoptysis, failure of the cavity to close after months of observation, spontaneous pneumothorax and inability to exclude neoplastic disease.

Churchill[99] has described the futility of resection in the presence of disseminated disease. In a case reported, the organisms could not be recovered from the sputum in spite of a widespread consolidation of the left upper lobe, with abscess formation. The patient had obviously no biologic defense against fungous infection. A skin test with coccidioidin was negative in this case, as well as in 12 of the 28 cases so tested in the series of Forbus and Bestebreurtje.[97]

Study and Morgenstern[100] have recently reported a case — the fourth so reported — of coexisting pulmonary coccidioidomycosis and tuberculosis.

Suppurative Disease

Lung Abscess

External drainage has gradually given way to primary lobectomy in the treatment of chronic lung abscess. Though at times life saving and occasionally the only possible surgical attack, external drainage in the past has been a relatively unsatisfactory compromise with a lethal "benign" disease. Sweet[101] has reviewed the experience at the Massachusetts General Hospital with lung abscess over two pre-penicillin five-year periods, 1933-1937 and 1938-1942. Each period included approximately the same number of cases (124 and 120, respectively). Comparing the two groups, he found that the curability rate rose from 49.2 to 59.2 per cent, whereas the mortality fell from 33.9 to 18.3 per cent.

The number cured spontaneously rose slightly, from 19.3 to 23.3 per cent, and the number cured by surgery from 29.9 to 35.8 per cent. The number of lobectomies increased from 6 primary and 11 secondary lobectomies to 15 primary and 11 secondary lobectomies. In the last five years at the same hospital, it is my impression that the proportion of lobectomies, particularly primary procedures, is far higher. In the 1938-1942 group, it is of interest that of 60 drainage cases, only 19 patients could be considered cured, 9 died, 11 had secondary lobectomy, and 21 were alive with disease, which in most cases meant a troublesome fistula and a pulmonary focus of considerable potential hazard.

Glover and Clagett[102] have reported 37 cases of chronic lung abscess treated by pulmonary resection at the Mayo Clinic for the ten-year period, January, 1937, through December, 1946. Among 21 lobectomies there was 1 death — a bilobectomy patient who died of shock with pulmonary edema forty-eight hours postoperatively. The final result in the remaining 20 cases was an asymptomatic cure. Of the 16 pneumonectomies in which the infection had been permitted to ravage an entire lung, the results were far different. Six patients died postoperatively, and an additional 3 died of brain abscess within five months of leaving the hospital. In another 2 cases empyema developed, 1 patient requiring subsequent thoracoplasty. An additional patient had sufficient cough and dyspnea to require thoracoplasty for correction of overexpansion and mediastinal shift. Thus, in 12 of the 16 cases in which the disease had had the upper hand, either death (9 cases) or serious complications (3 cases) followed surgical treatment. These results argue strongly for a surgical attack upon the lesion when lobectomy will suffice. Unfortunately, in an urban community, many of the patients have multilobar disease when first seen by any medical adviser.

Glover and Clagett have agreed with Neuhof and associates regarding early drainage before widespread secondary changes occur, and are not prepared to decide whether in a majority, or even a significant number of these patients, bronchiectatic changes will require extirpation. They have urged resection in cases in which secondary, presumably irreversible, changes have occurred; in those anatomically unsuited to drainage; in those associated with excessive bleeding; in children; in patients in whom cancer cannot be excluded; and in cases secondary to unremovable foreign bodies.

These indications agree essentially with Lindskog's[103] experience. He recommends primary resection without preliminary drainage as the procedure of choice in chronic lung abscess under the following conditions: multiple abscesses or extensive destruction in one or more lobes; secondary bronchiectasis; atelectasis and pneumonitis unrelieved by bronchoscopic treatment; uncontrolled bleeding; and perforation and localized empyema. He also reports 22 acute lung abscesses treated at the New Haven Hospital. On conservative therapy 5 patients were cured, and 3 much improved. After external drainage, 4 were cured and 4 much improved, and 1 died. Four patients required drainage of an empyema at the time of initial therapy, and 1 refused treatment.

It is probable that the place of early drainage of acute lung abscess needs redefinition if the powerful antibiotics now available can, by preventing invasive infection, reduce the amount of irreversible secondary change that converts an acute abscess into a chronic one. It is conceivable that the problem of lung abscess will resolve itself chiefly into a decision between nonoperative treatment and extirpation.

Brochiectasis

At a symposium held before the Massachusetts Medical Society in 1947 on the subject of bronchiectasis, Mallory[104] summarized the present theories of its pathogenesis. For each of five factors — direct bronchial infection, congenital malformation of the bronchial tree, bronchial stenosis, pulmonary atelectasis and pneumonitis — there is positive evidence of a causal relation, but none of the factors are constant or all-explanatory. He concluded that primary bronchitis and secondary atelectasis, with or without pneumonitis, could best explain the usual case, and that congenital cystic disease and bronchostenosis were relatively uncommon. The strategic point of attack, therefore, appears to be the prevention or prompt alleviation of atelectasis.

Carter and Welch[105] have recently presented a most interesting account of the development of bronchiectasis in 8 patients after the inhalation of a specific type of foreign body, — namely, a timothy head, — oriented stem downward. The report serves again to emphasize the respiratory hazards of childhood.

Surgical progress in bronchiectasis has been largely that of increasing safety and selectivity of operative procedures.[106, 107] More effective supportive measures, technical advances and extension of anatomic knowledge have contributed to the wider application of segmental resection and bilateral programs. There can be little doubt that penicillin has contributed greatly to the safety and ease of convalescence of these patients, and there is clinical evidence that aerosol penicillin may be of considerable help as a preoperative measure, particularly in patients producing copious amounts of sputum.[108, 109] Flooding of the airway under anesthesia has always been one of the major operative hazards.

King,[110] whose classic review of the subject has often been quoted to show the dismal future of bronchiectasis without surgical therapy, has recently commented[111] on the comparatively few patients seen nowadays that have the extensive

saccular disease upon which his report was based. He therefore injects a note of caution into the treatment of cases showing a maximal bronchographic extent of otherwise minimal disease.

The Esophagus

Cancer

A British surgeon recently reviewed the history of esophageal resection for carcinoma, and remarked how "the bold early experiments in esophageal surgery were followed by decades spent trying to circumvent, rather than face the dangers, and recently by a return to straightforward resection with anastomosis."[112] In the ten years since Adams and Phemister reported the first successful intrathoracic esophagogastrostomy for carcinoma, technics of esophageal resection in primary anastomosis have been standardized and so widely applied that a preliminary estimate of the efficacy of this, one of the latest fields of cancer, can be made. The June, 1948, issue of *Surgery* has been devoted to this subject, and contains excellent clinical characterizations of the disease, discussions of technics and editorial opinions of many of the leaders in the field. It is apparent that the majority are willing to abandon the Torek operation — credited with the first certain cure (in 1913) of carcinoma of the midesophagus — as inadequate for palliation and inefficient for cure. In support of this opinion, Sweet[113] has reported the total experience with the Torek procedure at the Massachusetts General Hospital. Of 14 patients 12 survived the removal of the tumor, but of these 4 died before construction of an antethoracic esophagus was begun, 4 died before the procedure was completed, 2 died after its completion, and 2 were surviving at the time of the report (four and two years, respectively).

Cancer of the esophagus differs from cancer of the lung in that its symptoms are generally so urgent that by far the great majority come to exploration, the age of the patient and his general condition notwithstanding. The distressing symptoms of slow starvation and the inability to swallow one's own saliva justify considerable operative risk and discomfort. The palliation afforded these patients if, at operation, resection and anastomosis are feasible has been deemed ample justification for the risks and surgical efforts involved, even if the prospect of cure is dim or nonexistent. Unfortunately, the anatomic relations of the esophagus make involvement of adjacent vital structures likely, though collected statistics indicate that the present resectability rate of 60 per cent of cases explored compares favorably with that of carcinomas elsewhere in the gastrointestinal tract. (To choose an example, 40 per cent of all gastric carcinomas seen at the Memorial Hospital are found to be resectable.[114]) Adding together the recorded experience of Sweet,[115] Garlock,[116] Strieder,[117] Clagett,[118] and Pack and McNeer,[114] which consist of total operative experience without revision by years, one finds that of 589 cases, 343 were resected, a rate of 58 per cent. Again, a compilation of the immediate operative mortality of low resection by the same group, in addition to the experience of deAmesti and Otaiza,[119] in Chile, and Lewis,[112] in Great Britain, yields 80 operative deaths in 303 cases — a rate of 26 per cent. The returns are, of course, incomplete, and show considerable variation between patients, but serve as a preliminary estimate of the surgical risk involved.

Carcinomas of the midesophagus requiring a high resection and usually an anastomosis at the level of the ante-aortic or supra-aortic arch should be distinguished from those demanding a low resection. The midzonal cancers represent patients for whom, until 1944, the Torek operation was the only generally accepted procedure. In that year, Garlock[120] and Sweet[113] independently reported their experience with resection and primary intrathoracic anastomosis for these high and difficult lesions. I have been unable to find a report of Garlock's over-all experience in this regard. However, Sweet[121] has recently recorded his in detail, and, as the number of cases is significant and the results represent the application of a uniform technic, his report may serve to characterize the current status of surgery of the midesophagus. In contrast to a mortality of 12 per cent in 109 cases of low resection, Sweet reports 17 postoperative deaths in 72 cases of midthoracic esophageal resection — a rate of 23.6 per cent. Of 50 such patients reported previously, 21 had infra-aortic anastomosis, with a mortality of 19 per cent, and 29 had supra-aortic anastomosis, with 24.1 per cent mortality. The significant portion of this mortality was attributable to cardiac disorders — not surprising in view of the magnitude of the procedures and the clinical characteristics of the patients. It was believed, however, that the cardiologist's advice regarding the use of quinidine, and the limitation of salt and fluid intake, did much to reduce this type of complication.

Quite apart from the immediate results of operation and the dramatic palliation it affords, there is some reason for optimism concerning ultimate results. Sweet has analyzed his cases from the point of view of survival. His figures indicate that the majority of deaths from metastasis or recurrence of the disease occurred during the first two years after operation. Of 30 patients who had resections of the lower esophagus or cardia more than three years before the report, 23 survived operation, and 9 were alive and clinically well at the time of writing (1 for seven, 2 for five, 2 for four, and 4 for three years after operation). From the point of view of survival, 82 per cent of patients who withstood the operation survived for six months, 48 per cent for a year, 44 per cent for eight months, and 31.5 per cent for two years. In most cases this

meant prolongation of life with relative comfort, for recurrence in the anastomotic site was uncommon. With this in mind it is difficult to agree with the following statement of Nielsen[122]:

> To us there is no doubt that the difficult task of trying to treat esophagus cancer both radically and symptomatologically will, to a very great extent, continue to be the domain of radiotherapy. All imaginable advances of thoracic surgery notwithstanding, only a small percentage of carcinomas in the esophagus will be amenable to surgical treatment, and the number of these in which a complete cure will be obtained will be smaller, still.

Nielsen has described an ingenious method of therapy, which delivers an effective amount of radiation to the tumor by rotating the patient vertically in the radiation field. Since the esophagus is an axial structure, the effective tumor dose is delivered with a minimum amount of radiation to any one area at the periphery. Of a total of 194 cases of carcinoma seen, only 8 were considered unsuitable for x-ray therapy. Of the 174 patients treated by rotation therapy, 140 received satisfactory tumor-dosage. Of those treated by rotation therapy, 25 per cent were alive in one year, and 15 per cent in two years. If one corrects Sweet's survival statistics to total number of cases resected and not merely those surviving operation and therefore having the opportunity to survive, 42 per cent were alive at one year, and 34 per cent survived for two years. The point is well taken, however, that in the nonresectable cases x-ray therapy may have palliative value. It is fair to state that the experience of others with x-ray therapy for carcinoma of the esophagus has not been so encouraging as that of Nielsen. Thus, Holmes and Schulz,[123] using supervoltage radiotherapy, found that only 8 per cent of patients survived for one year, and 2 per cent for two years.

Cancer of the cervical esophagus has stubbornly maintained the upper hand over surgical attack, although occasional successes in this region have been reported. Watson and Pool[124] have reviewed the historical aspect of the problem and made note of a twenty-three-year survival following surgical resection of a lesion of the cervical esophagus, reported by Evans in 1934, and a ten-year cure reported by Trotter in 1937. The authors themselves reported 2 cases ten years after combined surgical and x-ray therapy, and 1 case clinically free of disease seven years after surgical excision. Reviewing 77 cases of surgical esophageal cancer admitted to the Memorial Hospital from 1940 to 1947, they found that 22 per cent had clinically positive lymph nodes on admission. Survival after x-ray therapy averaged fifteen months in cases in which treatment failed to arrest the disease, but 3 patients treated more than fifteen months before the time of report were alive and well at that date. Of 7 patients treated by resection, 1 died within three months of operation, and the remainder were alive four, six, nine, twelve, thirty-six and eighty-four months, respectively. Using a similar operative approach Sweet[115] has reported 7 cases with excellent immediate results, but in each case, within six months to a year after operation, local recurrence or evidence of cervical-lymph-node metastasis became apparent. With 1 exception, all patients were dead at the time of his report.

The technic of cervical esophagectomy has been described in detail by Wookey,[125, 126] of Toronto. The procedure is designed to re-establish esophageal continuity at a second stage, and in many cases the larynx can be preserved. The operation, which is historically related to procedures described by Trotter and Eggers, consists of a block excision of the involved cervical esophagus.

Cancers in this area are almost invariably epidermoid, and the Memorial group,[114] at least, have believed that etiologically they bear a definite relation to chronic irritation in the oral cavity and to leukoplakia. As in other cancers, one of the major difficulties has been delay in diagnosis, occasioned chiefly by the surprising vagueness and lateness of symptoms of cancer in this region,—a scrapy throat, halitosis and ill defined discomfort on swallowing,—many of the ills often being ascribed to excessive smoking, postnasal drip or bad teeth. Pack[127] has decried the ritualistic aura surrounding the esophagoscope that has prevented its early and widespread use.

Perhaps the most difficult of all zones to resect, and fortunately the one least commonly involved in carcinoma, is the upper fourth of the thoracic esophagus. Cancer at the thoracic inlet is difficult of access, for both removal and reconstruction. Sweet[115] has reported a successful case in which, after removal of such a growth, an intracervical esophagogastrostomy was performed, the fundus of the stomach having been brought up through a defect in the upper thorax formed by resection of the inner end of the clavicle and first rib. Bricker and Burford[128] have recently described a pedicle tube flap for reconstruction of the upper esophagus following resection, with radical neck dissection and anterior thoracotomy.

Benign Obstructions

It is not surprising that heroic measures refined to a point of safety in the treatment of malignant lesions of the esophagus should be extended to include certain benign but often distressing conditions. Thus, although bougienage may be adequate for cicatricial obstruction resulting from chemical burn, in a variable number of patients it will be distasteful to the point of intolerability and occasionally impossible or extremely hazardous. Under these circumstances, resection and direct esophagogastric anastomosis seems logical, especially in the group of younger persons whose cardiopulmonary systems are sufficiently resilient.

Unfortunately many benign strictures extend high in the esophagus, occasionally well into the cervical region. At the time of the last progress report on this subject (1944) much interest was displayed in the procedure described by Yudin,[129] consisting of an anterior esophagus constructed from small intestine. Longmire[130] has recently described a modification of this maneuver by which, in patients having mesenteric vessels of inadequate length, blood supply is reconstituted by direct arterial and venous anastomosis to the internal mammary vessels. Longmire[131] has also presented an ingenious method of enclosing a segment of jejunum in a skin tube, which is then advanced onto the chest in multiple stages, in the course of which it is freed from its mesenteric blood supply. Rienhoff[132] has reported a method dividing the base of the mesentery of the small bowel so as to maintain the integrity of the vascular arcades. A sufficiently long segment of jejunum is thereby obtained, and can be brought well into the chest, permitting safe esophagojejunal anastomosis at a high level. Puestow and Chess[133] have described 4 cases of high resection and esophagogastric anastomosis, with 1 death. They employed the technic previously described by Sweet[134] and used by him for high strictures of the esophagus with very satisfactory results. Harrison[135] has reported 2 cases of lye stricture, both in three-year-old children, in whom esophageal continuity was re-established by a three-stage procedure, in which a single loop of jejunum was brought up intrathoracically to bridge the gap between the cervical esophagus and the stomach.

Of great current interest are cases of benign stricture of the lower portion of the esophagus in which the etiology is obscure. In these cases the esophagus is frequently shortened, and there may be associated peptic ulceration. Such cases are not to be confused with idiopathic dilatation of the esophagus (cardiospasm, achalasia), whose polyonomy reveals the confusion regarding its cause. Both the latter forms of benign lower esophageal obstruction are usually amenable to conservative measures, including instrumental dilatation. However, if these become burdensome to the patient or fail to achieve the desired functional results, a direct surgical attack is necessary.

In the idiopathic dilatation — cardiospasm-achalasia group — usually some form of pyloroplasty will suffice. Whether this is done transthoracically or transabdominally will depend on the preference of the operator.[136–143] The safety and versatility of the transthoracic approach has often been demonstrated, and is to be preferred when resection may be necessary.

Olsen and Harrington[144] have reported a series of 220 cases of esophageal hiatus hernia of the short-esophagus type. Eighty-nine of these had significant ulcerations of the esophagogastric junction, which could be controlled in the majority of cases by conservative therapy, including instrumental dilatation if obstruction was present. Abdominal operation in this group was unsatisfactory. The authors have discussed the etiology of peptic ulceration of the lower esophagus and drawn freely from the literature on the subject. Several interesting hypotheses are advanced to explain the short esophagus. They agree with Allison's[145] suggestion that peptic ulceration of the lower end of the esophagus may be the cause. The peptic ulceration may result from excessive or prolonged vomiting, or from constant bathing of the lower end of the esophagus in acid secretion, owing to incompetence of the physiologic sphincter of the cardia in association with hiatus hernia. The authors also refer to experimental evidence of Dey et al.,[146] who demonstrated reflex shortening of the esophagus on direct or indirect vagal stimulation. The latter might be translated to their 18 patients who had an associated duodenal ulcer, and 39 others with long histories of "dyspepsia."

Clark and Adams[147] have discussed transthoracic esophagogastrostomy in 5 cases of benign obstruction of the lower end of the esophagus after failure of conservative therapy. One of these patients had esophagitis associated with scleroderma; in 3 the etiology was obscure. No ulceration was described. Allison[145] has urged operative attack when conservative measures fail. When the peptic ulceration is accompanied by inefficiency of the diaphragm, which allows the stomach and abdominal esophagus to slide up into the mediastinum — a "landslide" type of hernia — he suggests that the length of the esophagus be restored, the stomach replaced in the abdomen, and the size of the hiatus corrected. When chronic ulceration and fibrosis make reduction of the anatomic deformity impossible, excision of this segment may be necessary.

Sweet[148] has reported 51 cases of repair of hiatus hernia by a transthoracic approach, which he favors because of the greater exposure obtained, the versatility of access and the freedom from complications. In the 51 cases described, intractable pain was the indication for operation in 68 per cent, incarceration in 18 per cent, and acute or chronic blood loss in 14 per cent. Soutter[149] has reviewed all the cases of surgical repair of hiatus hernia done at the Massachusetts General Hospital over the years and has concluded that the incidence of recurrence is lower and symptomatic relief greater after transthoracic rather than subdiaphragmatic repair.

In the course of a comprehensive review of the subject of diaphragmatic hernia, Harrington[150] has discussed the many aspects of the problem and has reviewed his experience with 404 cases treated surgically. Two hundred and eighty-seven of these were esophageal hiatus hernias, for which he preferred an abdominal approach to the defect, usually preceded by a temporary phrenic paralysis.

In conclusion, a final word might be added — namely, the obvious importance of ruling out cancer in cases considered to be benign obstruction. To this end, the combination of careful x-ray study and esophagoscopic examination is necessary, and often must be repeated before cancer can be ruled out beyond reasonable doubt.

Congenital Atresia

At the other end of the time scale from resection of the esophagus for carcinoma is an equally formidable operative procedure for the correction of esophageal atresia and tracheoesophageal fistula. Haight,[151] who is credited with the first successful direct anastomosis of the esophagus in 1941 (there were several near misses just prior to that time, notably Shaw's case in 1939), has recently reported 52 cases in which an effort was made to restore esophageal continuity. In 11 of the 52 patients an esophageal anastomosis was not possible, and in another patient it was not done. In 1 of these cases an esophagogastric anastomosis was done by Dr. F. X. Byron. Of 40 patients for whom an esophageal anastomosis was completed, 22 died, and 18 recovered — a recovery rate of 45 per cent. The over-all recovery rate in the 52 patients explored was 34.6 per cent. Haight and his associates favor a right extrapleural exposure of the anomaly, particularly if the preoperative x-ray film demonstrates air in the stomach — a sign that there should be a sufficient length of the two segments to permit anastomosis. When air is not present in the stomach before operation, agenesis of the lower esophagus is commonly found, and direct end-to-end anastomosis of the esophagus is impossible. Haight[15] had previously emphasized the great difficulty in securing a suture line without tension since swallowing and crying, after the effects of the anesthesia have worn off, tend to raise the upper portion of the esophagus, and the descent of the diaphragm on inspiration exerts traction downward.

Ladd and Swenson[153, 154] have reported experience with this disease at the Children's Hospital and suggested a new classification of the anomaly to supersede that of Vogt. Thirty-nine primary anastomoses were carried out, with 20 recoveries. Forty-three multiple-stage procedures produced 16 living patients, of whom 5 subsequently had an antethoracic esophagus completed. Their experience with a transpleural approach was disheartening: 4 deaths out of 5 attempts. Swenson[154] has recommended a two-layer, watertight interrupted-fine-silk anastomosis, and reports only one fistula in 15 patients, and this closed spontaneously.

In the occasional case in which, for anatomic reasons, direct anastomosis is not possible, a multiple-stage procedure may be considered, aiming first at the closure of the tracheoesophageal fistula, cervical esophagostomy, ligation of the lower esophageal segment, some form of gastrostomy, and finally reconstruction of an anterior esophagus. As Lam[155] has demonstrated, the last may require great persistence in the face of many discouragements. Sweet[156] has attacked the problem successfully in 2 children who had esophagostomy and gastrostomy early in infancy as a life-saving measure. He subsequently performed a successful intracervical esophagogastrostomy after advancing the stomach through the chest, posterior to the hilus and out through a new thoracic inlet formed by resection of the inner end of the clavicle and first rib.

Pulmonary complications have been a limiting factor in the surgical correction of this major developmental anomaly. For this reason, the use of small amounts of lipiodol are much to be preferred over barium at the time of x-ray examination. Furthermore, because of the danger of spilling over into the tracheobronchial tree, operative intervention should not be postponed beyond the minimum time necessary to attend to the physiologic needs of the infant.

Miscellaneous Considerations

Surgery of the heart and great vessels qualifies for a progress report in its own right and will not be considered here. However, a rather closely related entity, variously called pulmonary arteriovenous aneurysm,[157] pulmonary cavernous hemangioma,[158] hemangioma of the lung[159] and arteriovenous fistula of the lung,[160] has been the subject of many recent reports. As the names imply, this lesion furnishes a vascular shunt across the pulmonary circuit so that deficient oxygenation of the systemic arterial blood results. On the basis of this deficiency, with its clinical manifestations of cyanosis, clubbing and polycythemia, in addition to the finding of a lung tumor that emits a bruit, the diagnosis can be made. Dramatic improvement has followed lobectomy in the cases reported.

Mediastinal tumors continue to be a source of never-ending speculation. Maier[161] has reviewed the problem of bronchogenic cysts of the mediastinum and recorded 8 additional cases. Within the past year, Byron, Alling and Samson[162] have each had a case of intrathoracic meningocele that presented as a smooth outlined and lobulated posterior mediastinal mass. Review of their cases, as well as the 5 previously recorded in the literature, showed that the lesion is frequently associated with widening of the intervertebral foramens, erosion of the rib and vertebra and even diffuse neurofibromatosis. Since excision of the meningocele is usually deemed inadvisable or impossible, they have suggested the use of a contrast medium intraspinally in the x-ray differential diagnosis.

Watson and James[163] and Maier[164] have described the management of large defects of the chest wall. The former have suggested a large fascia-lata graft, and in 1 patient, who died of pulmonary embolism eighteen days after such a repair, they found that

the graft had taken well to the diaphragm and pleura.

Asthma continues to be a relatively undiscovered country for the thoracic surgeon. In 1948, Carr and Chandler[165] reported 5 patients in whom encouraging clinical results followed post-ganglionic resection of the upper dorsal sympathetic ganglions. In discussion of their report, Abbott pointed out that he and his associates approached the problem by an attack on the parasympathetic system. Similar conflicting clinical evidence was added by Adams. The problem awaits definition of the pathologic changes and disturbances of physiology under attack, and the relation of the lung to the autonomic nervous system.

References

70. Björk, V. O. Bronchiogenic carcinoma. *Acta chir. Scandinav.* **95** (Supp. 123):1-113, 1947.
71. Ochsner, A., DeBakey, M. E., and Dixon, L. Primary pulmonary malignancy treated by resection: analysis of 129 cases. *Ann. Surg.* **125**:522-540, 1947.
72. Rienhoff, W. F. Present status of surgical treatment of carcinoma of lung. *Ann. Surg.* **125**:541-565, 1947.
73. Jones, J. C. Surgical aspects of bronchogenic carcinoma. *J. A. M. A.* **134**:113-117, 1947.
74. Adams, R. Carcinoma of lung: factors affecting survival after resection of cancer of lung. *J. Thoracic Surg.* **17**:306-322, 1948.
75. Graham, E. A. Discussion of Adams.[74]
76. Coleman, F. P. Primary carcinoma of lung, with invasion of ribs: pneumonectomy and simultaneous block resection of chest wall. *Ann. Surg.* **126**:156-168, 1947.
77. Adams, R. Primary lung tumors. *J. A. M. A.* **130**:547-553, 1946.
78. Neuhof, H., and Aufses, A. H. Cancer of lung: interval and late results of operation in relation to topography and gross pathology. *J. Thoracic Surg.* **17**:297-305, 1948.
79. Head, J. R. Discussion of Adams.[74]
80. Janes, R. M. Lipoid pneumonia simulating bronchogenic carcinoma. *J. Thoracic Surg.* **16**:451-457, 1947.
81. Nelson, H. P. Tracheo-bronchial lymphatic glands. *J. Anat.* **66**: 228-241, 1932.
82. Birath, G., Crafoord, C., and Rudström, P. Pulmonary function after pneumonectomy and lobectomy. *J. Thoracic Surg.* **16**:492-511, 1947.
83. Cournand, A., and Berry, F. B. Effect of pneumonectomy upon cardiopulmonary function in adult patients. *Ann. Surg.* **116**: 532-552, 1942.
84. Bateman, J. B. Measurement of intrapulmonary mixing and pulmonary midcapacity ("functional residual air"). *Proc. Staff Meet., Mayo Clin.* **21**:112-120, 1946.
85. Widmann, B. P. Roentgen therapy for bronchiogenic cancer. *Am. J. Roentgenol.* **51**:61-69, 1944.
86. Leddy, E. T., and Moersch, H. J. Roentgen therapy for bronchiogenic carcinoma. *J. A. M. A.* **115**:2239-2242, 1940.
87. Shorvon, L. M. Carcinoma of bronchus with especial reference to its treatment by radiotherapy. *Brit. J. Radiol.* **20**:443-449, 1947.
88. Hocker, A. F., and Guttman, R. J. Three and one-half years' experience with 1000 kilovolt roentgen therapy unit at Memorial Hospital. *Am. J. Roentgenol.* **51**:83-94, 1944.
89. Alexander, J., and Haight, C. Pulmonary resection for solitary metastatic sarcomas and carcinomas. *Surg., Gynec. & Obst.* **85**: 129-146, 1947.
90. Effler, D. B., and Blades, B. Surgical treatment of solitary lung metastasis. *J. Thoracic Surg.* **17**:27-37, 1948.
91. Strieder, J. W. Thoracic surgery. *New Eng. J. Med.* **231**:360-366 and 388-396, 1944.
92. Streptomycin in the Treatment of Tuberculosis. Report to Council on Pharmacy and Chemistry of American Medical Association by Streptomycin Committee on the Veterans Administration, 1948.
93. Chapman, P. T., O'Brien, E. J., and O'Rourke, P. V. Role of streptomycin in surgical treatment of pulmonary tuberculosis. Paper presented at meeting of American Association for Thoracic Surgery, 1948.
94. Sweet, R. H. Lobectomy and pneumonectomy in treatment of pulmonary tuberculosis. *J. Thoracic Surg.* **15**:373-383, 1946.
95. Churchill, E. D., and Klopstock, R. Lobectomy for pulmonary tuberculosis. *Ann. Surg.* **117**:641-649, 1943.
96. Overholt, R. H., Langer, L., Szypulski, J. T., and Wilson, N. J. Pulmonary resection in treatment of tuberculosis: present-day technique and results. *J. Thoracic Surg.* **15**:384-413, 1946.
97. Forbus, W. D., and Bestebreurtje, A. M. Coccidioidomycosis: study of 95 cases of disseminated type with special reference to pathogenesis of disease. *Mil. Surgeon* **99**:653-719, 1946.
98. Greer, S. J., Forsee, J. H., and Mahon, H. W. Surgical management of pulmonary coccidioidomycosis in focalised lesions. Paper presented at meeting of American Association for Thoracic Surgery, 1948.
99. Churchill, E. D. Malignant lymphoma of lung and pulmonary coccidioidomycosis: clinic on surgical lesions of lung with consolidation. *S. Clin. North America* **27**:1113-1120, 1947.
100. Study, R. S., and Morgenstern, P. Coexisting pulmonary coccidioidomycosis and tuberculosis. *New Eng. J. Med.* **238**:837, 1948.
101. Sweet, R. H. Analysis of Massachusetts General Hospital cases of lung abscess from 1938 through 1942. *Surg., Gynec. & Obst.* **80**: 568-574, 1945.
102. Glover, R. P., and Clagett, O. T. Pulmonary resection for abscess of lung. *Surg., Gynec. & Obst.* **86**:385-394, 1948.
103. Lindskog, G. E. Surgical treatment of chronic pulmonary abscess. *Surgery* **15**:783-788, 1944.
104. Mallory, T. B. Pathogenesis of bronchiectasis. *New Eng. J. Med.* **237**:795-798, 1947.
105. Carter, M. G., and Welch, K. J. Bronchiectasis following aspiration of timothy grass: report of eight cases. *New Eng. J. Med.* **238**: 832-836, 1948.
106. Strieder, J. W. Surgical aspects of bronchiectasis. *New Eng. J. Med.* **238**:109-112, 1948.
107. Meade, R. H., Jr., Kay, E. B., and Hughes, F. A. Report of one hundred and ninety-six lobectomies performed at Kennedy General Hospital Chest Surgical Center from 1943 to 1946 with one death. *J. Thoracic Surg.* **16**:16-29, 1947.
108. Findlay, C. W., Jr., and Sweet, R. H. Aerosol penicillin as therapeutic adjunct in preparation of patients with suppuration of lung for pulmonary resection. *J. Thoracic Surg.* **16**:81-90, 1947.
109. Donnelly, J. H., Phillips, F. J., Bartlett, J. P., and Adams, W. E. Evaluation of methods of penicillin therapy in thoracic surgery. *Ann. Surg.* **126**:579-591, 1947.
110. Perry, K. M. A., and King, D. S. Bronchiectasis: study of prognosis based on follow-up of 400 patients. *Am. Rev. Tuberc.* **41**:531-548, 1940.
111. King, D. S. Personal communication.
112. Lewis, I. Surgical treatment of carcinoma of oesophagus, with special reference to new operation for growths of middle third. *Brit. J. Surg.* **34**:18-31, 1946.
113. Sweet, R. H. Surgical management of carcinoma of midthoracic esophagus: preliminary report. *New Eng. J. Med.* **233**:1-7, 1945.
114. Pack, G. T., and McNeer, G. Surgical treatment of cancers of gastric cardia. *Surgery* **23**:976-1019, 1948.
115. Sweet, R. H. Treatment of carcinoma of esophagus and cardiac end of stomach by surgical extirpation. *Surgery* **23**:952-975, 1948.
116. Garlock, J. H. Causes of mortality following radical resection of esophagus for carcinoma. *J. Thoracic Surg.* **13**:415-423, 1944.
117. Strieder, J. W. Surgical management of carcinoma of lower two-thirds of esophagus and cardiac end of stomach. *J. Thoracic Surg.* **17**:143-161, 1948.
118. Payne, J. H., and Clagett, O. T. Transthoracic gastric resection for lesions of cardia of stomach and lower part of esophagus. *Surgery* **23**:912-920, 1948.
119. deAmesti, F. D., and Otaiza, E. Cardioesophageal cancers treated via transthoracic and transdiaphragmatic route. *Surgery* **23**:921-934, 1948.
120. Garlock, J. H. Re-establishment of esophagogastric continuity following resection of esophagus for carcinoma of middle third. *Surg., Gynec. & Obst.* **78**:23-28, 1944.
121. Sweet, R. H. Carcinoma of esophagus and cardiac end of stomach: immediate and late results of treatment by resection and primary esophagogastric anastomosis. *J. A. M. A.* **135**:485-490, 1947.
122. Nielsen, J. Clinical results with rotation therapy in cancer of esophagus: preliminary report based on 174 cases. *Acta radiol.* **26**: 361-389, 1945.
123. Holmes, G. W., and Schulz, M. D. Supervoltage radiation: review of cases treated during eight year period (1937-1944 inclusive). *Am. J. Roentgenol.* **55**:533-554, 1946.
124. Watson, W. L., and Pool, J. L. Cancer of cervical esophagus: discussion of treatment. *Surgery* **23**:893-905, 1948.
125. Wookey, H. Surgical treatment of carcinoma of pharynx and upper esophagus. *Surg., Gynec. & Obst.* **75**:499-506, 1942.
126. *Idem.* Surgical treatment of carcinoma of hypopharynx and oesophagus. *Brit. J. Surg.* **35**:249-256, 1948.
127. Pack, G. T. Introduction to symposium on cancer of esophagus and gastric cardia. *Surgery* **23**:867-873, 1948.
128. Bricker, E., and Burford, T. H. Use of pedicle tube flap in carcinoma of upper esophagus. Paper presented at meeting of American Association for Thoracic Surgery, 1948.
129. Yudin, S. S. Surgical construction of 80 cases of artificial esophagus. *Surg., Gynec. & Obst.* **78**:561-583, 1944.
130. Longmire, W. P., Jr. Modification of Roux technique for antethoracic esophageal reconstruction: anastomosis of mesenteric and internal mammary blood vessels. *Surgery* **22**:94-100, 1947.
131. Longmire, W. P., Jr., and Ravitch, M. M. New method for constructing artificial esophagus. *Ann. Surg.* **123**:819-835, 1946.
132. Rienhoff, W. F., Jr. Intrathoracic esophagojejunostomy for lesions of upper third of esophagus. *South. M. J.* **39**:928-940, 1946.
133. Puestow, C. B., and Chess, S. J. Resection of esophagus for persistent stricture. *Arch. Surg.* **56**:34-47, 1948.
134. Sweet, R. H. Subtotal esophagectomy with high intrathoracic esophagogastric anastomosis in treatment of extensive cicatricial obliteration of esophagus. *Surg., Gynec. & Obst.* **83**:417-427, 1946.
135. Harrison, A. W. Transthoracic esophagojejunogastrostomy for high stricture of esophagus. Paper presented at meeting of American Association for Thoracic Surgery, 1948.

136. Ochsner, A., and Debakey, M. Surgical considerations of achalasia: review of literature and report of three cases. *Arch. Surg.* **41**:1146-1183, 1940.

137. Clagett, O. T., Moersch, H. J., and Fisher, A. Esophagogastrostomy in treatment of cardiospasm. *Surg., Gynec. & Obst.* **81**:440-445, 1945.

138. Schiebel, H. M. Treatment of esophageal achalasia or cardiospasm: report of four patients treated surgically. *Surgery* **20**:558-570, 1946.

139. Grimson, K. S., Reeves, R. J., Trent, J. C., and Wilson, A. D. Treatment of patients with achalasia by esophagogastrostomy. *Surgery* **20**:94-103, 1946.

140. Sweet, R. H. Idiopathic dilatation of esophagus. *S. Clin. North America* **27**:1128-1135, 1947.

141. Kay, E. B. Surgical treatment of cardiospasm. *Ann. Surg.* **127**: 34-39, 1948.

142. Gill, D. C., and Child, C. G., III. Esophagogastrostomy in treatment of cardiospasm. *Surgery* **23**:571-583, 1948.

143. Scott, W. J. M. Idiopathic dilation of esophagus: differentiation of clinical types and successful operation in intractable cases. *Ann. Surg.* **122**:582-605, 1945.

144. Olsen, A. M., and Harrington, S. W. Esophageal hiatal hernias of short esophagus type: etiologic and therapeutic considerations. *J. Thoracic Surg.* **17**:189-209, 1948.

145. Allison, P. R. Peptic ulcer of esophagus. *J. Thoracic Surg.* **15**:308-317, 1946.

146. Dey, F. L., Gilbert, N. C., Trump, R., and Roskelley, R. C. Reflex shortening of esophagus in experimental animal with production of esophageal hiatus hernia. *J. Lab. & Clin. Med.* **31**:499-506, 1946.

147. Clark, D. E., and Adams, W. E. Transthoracic esophagogastrostomy for benign strictures of lower esophagus. *Ann. Surg.* **122**:942-953, 1945.

148. Sweet, R. H. Repair of hiatus hernia of diaphragm by supradiaphragmatic approach: technic and results. *New Eng. J. Med.* **238**:649-653, 1948.

149. Soutter, L. Analysis of cases of hiatus hernia treated by surgery at Massachusetts General Hospital. *S. Clin. North America* **27**:1121-1127, 1947.

150. Harrington, S. W. Surgical treatment of more common types of diaphragmatic hernia: esophageal hiatus, traumatic, pleuroperitoneal hiatus, congenital absence and foramen of Morgagni: report of 404 cases. *Ann. Surg.* **122**:546-568,1945.

151. Haight, C. Discussion of Lyon, G., and Johnson, S. G. Discussion of congenital esophageal atresia and tracheoesophageal fistula. *J. Thoracic Surg.* **17**:162-177, 1948.

152. *Idem.* Congenital atresia of esophagus with tracheoesophageal fistula. *Ann. Surg.* **120**:623-655, 1944.

153. Ladd, W. E., and Swenson, O. Esophageal atresia and tracheoesophageal fistula. *Ann. Surg.* **125**:23-40, 1947.

154. Swenson, O. End-to-end anastomosis of esophagus for esophageal atresia. *Surgery* **22**:324-334, 1947.

155. Lam, C. R. Further experiences in surgical treatment of congenital atresia of esophagus with tracheo-esophageal fistula. *Surgery* **20**: 174-179, 1946.

156. Sweet, R. H. New method of restoring continuity of alimentary canal in cases of congenital atresia of esophagus with tracheoesophageal fistula not treated by immediate primary anastomosis. *Ann. Surg.* **127**:757-768, 1948.

157. Watson, W. L. Pulmonary arteriovenous aneurysm: new surgical disease. *Surgery* **22**:919-929, 1947.

158. Bisgard, J. D. Pulmonary cavernous hemangioma with arteriovenous fistula, surgical management: case report. *Ann. Surg.* **126**: 965-972, 1947.

159. Wodehouse, G. E. Hemangioma of lung: review of four cases, including two not previously reported, one of which was complicated by brain abscess due to *H. influenzae*. *J. Thoracic Surg.* **17**:408-415, 1948.

160. Maier, H. C., Hummelstein, A., Riley, R. L., and Bunin, J. J. Arteriovenous fistula of lung. *J. Thoracic Surg.* **17**:13-26, 1948.

161. Maier, H. C. Bronchiogenic cysts of mediastinum. *Ann. Surg.* **127**: 476-502, 1948.

162. Byron, F. X., Alling, E. E., and Samson, P. C. Intrathoracic meningocele. Paper presented at meeting of American Association for Thoracic Surgery, 1948.

163. Watson, W. L., and James, A. G. Fascia lata grafts for chest wall defects. *J. Thoracic Surg.* **16**:399-406, 1947.

164. Maier, H. C. Surgical management of large defects of thoracic wall. *Surgery* **22**:169-178, 1947.

165. Carr, D., and Chandler, H. Dorsal sympathetic ganglionectomy for intractable asthma. *J. Thoracic Surg.* **17**:1-12, 1948.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 34511*

PRESENTATION OF CASE

First admission. A sixty-two-year-old Negro janitor entered the hospital complaining of left-upper-quadrant pain of three weeks' duration.

Five months previously the patient developed a nonradiating, dull pain in the left upper quadrant, which responded quickly to the bland diet on which he was placed. Recurring three weeks before admission this pain became increasingly severe and was especially bad after the evening meal and during the night. He had no other digestive complaints except mild constipation. There was a 20-pound weight loss during these three weeks.

Nineteen years before admission he had had an excision of the cecum and appendix, with side-to-side ileocolostomy for diverticulitis of the cecum. Eight years before admission he received a one-year course of intramuscular injections following the detection of a positive serologic test at another hospital. He had been aware of high blood pressure and a heart murmur for two years, without specific cardiovascular symptoms. He had an increase of nocturia from one to four or five times during the month before entry.

Physical examination showed a tall, thin man who had water-hammer pulses, a blood pressure of 210 systolic, 50 diastolic, and a heart enlarged to the sixth interspace in the anterior axillary line. The aortic second sound was increased over the pulmonic second sound. Grade III aortic diastolic and Grade I apical systolic murmurs were heard. The abdominal aorta was prominent. No masses were felt.

Examination of the blood revealed a white-cell count of 7400, with 80 per cent neutrophils. The hemoglobin was 13 gm. A blood Hinton test was negative. The urine concentrated to 1.028 and gave a + test for albumin, and there was a rare red blood cell, white blood cell and cellular cast per high-power field. The stool was guaiac negative.

*Presented at a meeting of the New England Cancer Society held at the Massachusetts General Hospital.

A barium enema, gastrointestinal series and films of the spine were reported normal. X-ray films of the chest showed cardiac enlargement, a possible dilatation of the ascending aorta and wide aortic pulsations. The serum nonprotein nitrogen was 23 mg. and the sugar 106 mg. per 100 cc. The prothrombin time was 18 seconds (normal, 17 seconds). The amylase was 32 units per 100 cc. and the serum albumin 4.6 gm., and the globulin 3.7 gm. per 100 cc., giving an albumin-globulin ratio of 1:26. The urine culture was negative. A lumbar puncture was not remarkable; the Wassermann reaction was negative, and the spinal-fluid protein was 38 mg. per 100 cc. An electrocardiogram was not diagnostic.

The patient had several severe attacks of left-upper-quadrant pain while on the ward without definite relation to food intake or defecation. During one such typical episode he was found sitting in bed hunched over a bed table. Deep palpation of the abdomen revealed acute tenderness just to the left of the umbilicus, and there was a sense of resistance to palpation without detection of a definite mass in the area. Neither nitroglycerin nor sodium bicarbonate gave any relief. He was discharged to be followed in the Out-Patient Department.

Final admission (two weeks later). The patient returned to the hospital by ambulance, having been bed ridden at home. He appeared dehydrated and emaciated and gave a history of continued, severe, nonradiating, left-upper-quadrant pain since discharge. On two or three occasions he had vomited, with temporary relief of pain. In addition he appeared weaker.

Physical examination was the same as on the previous admission, except the liver was felt to descend three fingerbreadths on deep inspiration. An intravenous pyelogram and a left retrograde pyelogram were negative. Sigmoidoscopy to 16 cm. was normal. The stool was guaiac positive on four of seven occasions. The urine concentrated to 1.027 and gave a + test for albumin, and there were 20 white cells, 5 red cells and occasional casts per high-power field in the sediment. The hemoglobin was 10.5 gm. The white-cell count was 8000, with 20 per cent myelocytes and myeloblasts. A hematologic consultant found myeloid hyperplasia on the smear and sternal biopsy. The serum lipase was 1.2 mg., and the nonprotein nitrogen 38 mg. per 100 cc. The van den Bergh reaction was negative; the cephalin flocculation test was negative. The calcium was 9.6 mg., and the phosphorus 4.6 mg. per 100 cc., and the alkaline phosphatase 6.6 Bodansky units.

The patient was prepared for exploration by 12 gm. of sulfasuxidine and 2 gm. of sulfadiazine daily (as urinary antiseptic), transfusion and Miller–Abbott intubation. The white-cell count rose to 13,400 on the thirteenth hospital day, when a urine culture was positive for colon bacilli and *Staphylococcus aureus*. On the seventeenth hospital day he was drowsy, and an emergency nonprotein nitrogen was 116 mg. per 100 cc. The operation was cancelled, and the Miller–Abbott tube withdrawn. He continued to be lethargic and apathetic, and at 1:30 a.m. of the eighteenth day he went into sudden collapse and died.

Differential Diagnosis

Dr. Richard B. Cattell*: This man's past history evidently had little to do with the present findings and complaints. There are two things that we can begin with in this case: he was in the cancer age, at sixty-two, and this is supposed to be a conference for the New England Cancer Society. I think Dr. Cabot always said that if one is frequently out on a limb the percentage diagnosis is the one to take. We will assume it is cancer.

In the past history it is stated that he had a diverticulum of the cecum. This is exceedingly rare. Dr. Castleman will tell you how many cases they have in their files.

Dr. Benjamin Castleman: I do not believe I have ever seen one.

Dr. Cattell: That bears out my impression. This man had syphilis, syphilitic heart disease, aortic regurgitation and hypertensive heart disease and probably, as indicated by the x-ray film, dilatation of the aorta. He did not have a palpable mass at any time. He could localize the symptoms in the left upper quadrant, and there are certainly lesions that occur in this region. The findings in the gastrointestinal tract were all negative except for guaiac-positive stools on the second examination, which should exclude involvement of the stomach or colon, although a positive guaiac reaction can occur without an actual ulcerative lesion. On this admission there was a new blood finding — myeloblasts were found in the sternal marrow. This was a terminal blood condition and was not, in my opinion, myeloblastic leukemia, although that is a definite possibility.

I think from all we have pointed out here in the way of symptoms that we have a lesion in the retroperitoneal area, probably not involving the pancreas, or if it did involve the body or tail of the pancreas, it extended to involve other organs as it became progressive. With carcinoma of the body of the pancreas "in the silent area" where few symptoms are produced, the commonest symptom in our experience is pain in the back, not in the left upper quadrant but in the back, that usually passes over to involve the other side. The second group of symptoms is entirely missing in this history, and that is the usual presence of bowel symptoms, which are characteristic of any pancreatic lesion that involves and obstructs the duct of Wirsung. We have had 165 carcinomas of the pancreas since

*Member, Department of Surgery, Lahey Clinic, Boston.

August, 1942. They usually begin with bowel symptoms caused by decreased pancreatic enzymes available in the bowel. No bowel symptoms were present in this patient, but this is possible with carcinoma of the body and tail, particularly if a portion of the pancreas remains available to furnish the external pancreatic enzymes through the duct of Wirsung into the duodenum. I do not believe we have an ulcerative lesion that involves or invades the gastrointestinal tract, although one can see this with a lesion in this location, with involvement of the first portion of the jejunum as well as the more common lesions of the pancreas that ulcerate into the second portion of the duodenum. There are some things inconsistent with pancreatic primary neoplasm. There is no evidence that this was one of the tumors arising in the islands of Langerhans. There was no change in metabolism of glucose. About 30 per cent of these were carcinoma in our experience at the time the patients were operated on. So we would consider this to be a primary lesion arising in the tail or body of the pancreas, with gradual extension. The pain of carcinoma of the pancreatic body may be relieved by leaning forward and is characteristically found. Whoever saw this patient and took this history was impressed with that one clinical fact.

The other diagnosis we have to consider is kidney neoplasm. This can reasonably be excluded. Would you like to show the x-ray films?

Dr. Castleman: The only x-ray films available are those taken between the first and second admissions and these are all normal.

Dr. Cattell: A definitely ulcerated lesion in the region of the ampulla of Vater may occasionally be demonstrated by roentgenographic means. In carcinoma of the body of the pancreas one may see displacement of the stomach upward, and sometimes can see evidence of displacement of the ligament of Treitz. If this is a large retroperitoneal tumor, the commonest ones are neurofibroma, fibrosarcoma, leiomyosarcoma and lipomyosarcoma. We ought to be able to feel a mass and see displacement of the kidney, stomach, small bowel or colon. I do not believe this is a retroperitoneal tumor because of the rapid progression to death.

Dr. Ralph E. Miller: What do you think this blood picture was due to?

Dr. Cattell: I know very little about hematologic findings. I would think it was a terminal state in a failing patient due to marked stimulation of the marrow. I do not believe he had a myelogenous leukemia.

Dr. Miller: Do you think it consistent with extreme metastases to the liver from a carcinoma?

Dr. Cattell: I do not believe so from the findings, although it might well be.

Dr. Grantley W. Taylor: Did you consider an aortic aneurysm in the differential diagnosis? He had a background of syphilis.

Dr. Cattell: As I read the report I considered it seriously but threw it out on the basis of my first remarks.

A Physician: How about the barium enema? Was that negative?

Dr. Castleman: It was reported as negative.

A Physician: On the first admission?

Dr. Castleman: Yes.

Dr. Knowles B. Lawrence: I would suggest carcinoma of the splenic flexure with complications.

Dr. Cattell: That is a definite possibility, but the barium enema was negative.

Dr. Thomas J. Anglem: For how many days was sulfadiazine given?

Dr. Castleman: For six days during the last admission.

Dr. Joseph Ross: Is there any implication of the report of myeloid hyperplasia at the biopsy?

Dr. Castleman: I think it meant hyperplasia of the myeloid elements but no myeloma.

Dr. Cattell: That was my interpretation.

Dr. Castleman: Just a shift to the left.

Clinical Diagnosis

Carcinoma of pancreas.

Dr. Cattell's Diagnosis

Carcinoma of body of pancreas.

Anatomical Diagnoses

Retroperitoneal fibrosarcoma, bilateral, with involvement of both adrenal glands and with metastases to liver and stomach.

Chordoma of lumbar vertebras.

Pathological Discussion

Dr. Castleman: The clinical impression was the same as Dr. Cattell's: that the patient had carcinoma of the pancreas. One opinion reads as follows:

> This sixty-two-year-old man with syphilitic heart disease has left-upper-quadrant pain of about two months' duration, associated with weight loss and occasional vomiting. All x-ray examinations have failed to disclose the site of the lesion in the abdomen, so the tail of the pancreas has been considered as the site of a neoplasm. The history of constipation of two years' duration, worse in recent months, suggests a colonic lesion (carcinoma of the splenic flexure), but the barium enema was negative. I agree that laparotomy is now indicated and will not be surprised to find a retroperitoneal tumor in the left upper quadrant, with possibly a lymphoma, or no intra-abdominal disease.

At autopsy the patient had a retroperitoneal tumor, a very malignant tumor, and its distribution was rather unusual. It involved both sides of the abdomen. The larger mass was located in the region of the right adrenal gland, completely obliterating it, and extending into the liver on that side as well as invading into a portion of the terminal ileum. There was a similar but smaller tumor on the left side involving a portion of the left adrenal gland and extending into the tissues around that

region. There was also a metastasis within the liver and one to the serosa of the stomach. On microscopical section the cells tended to be quite spindle shaped and in some places were composed of dense collagen. The appearance was most consistent with a fibrosarcoma, probably of neurogenic origin, that had involved both sides of the abdomen. The cells in many places were very atypical with numerous mitoses, and it seems to me that he could not have had a tumor as wild as this for a long time. The fact that the tumor occurred on both sides would be in favor of some form of neurogenic tumor, perhaps arising from neurofibromas. There were no metastases to the lung. Pressure on the ureters perhaps accounted for some degree of the pyelonephritis and probably was the cause of the elevated nonprotein nitrogen toward the end. An incidental finding was the presence in the second and third lumbar vertebras of grayish-white tissue, not at all connected with the tumor in the retroperitoneal space, that the prosector thought was another metastasis but, on microscopical examination, proved to be a chordoma. It was just picked up on routine sectioning of the vertebral column. I do not believe it produced any symptoms. I wonder if Dr. Robbins can possibly see it in these x-ray films.

DR. LAURENCE L. ROBBINS: Certainly the density of the lumbar vertebras is increased, but I do not remember a chordoma doing that.

DR. CASTLEMAN: It was very soft.

DR. ROBBINS: I would not be able to make a definite diagnosis of the lesion.

DR. CATTELL: You cannot see anything in the right or left adrenal gland?

DR. ROBBINS: No.

CASE 34512

PRESENTATION OF CASE

First admission. A thirteen-year-old girl was admitted to the hospital complaining of a dry, persistent cough.

At the onset of the dry cough three years before admission nasal polyps were found. The cough continued following polypectomy. Several months later her tonsils and adenoids were removed, as were recurrent nasal polyps, without improving the chronic cough. Ten weeks before admission the cough became severe and was accompanied by large amounts of greenish-yellow, foul-smelling sputum. Vomiting followed severe paroxysms of coughing. She complained of headache and abdominal pain. She lost 13 pounds during this period. Five days before admission the temperature was 102°F.

The patient was the fifth of five children. Two older siblings, twenty-six and seventeen years old, were well. One sibling had died at the age of eight months from pneumonia, which had been present for a long time. Another had died at the age of eight weeks of vomiting, which had been present since birth.

The patient had been born at term following an uneventful pregnancy. The birth weight was 9¾ pounds. Development during the first ten years of life was similar to that of her siblings except that she was slightly obese. Since infancy she had been a voracious eater, and the stools were always large and bulky. She had had measles, chicken pox, mumps and German measles, and in each case apparently recovered without aftereffects. She had annual winter colds with cough from early childhood on, which tended to last all winter and were more severe than the other siblings' colds.

Physical examination showed a poorly developed and undernourished girl, with wasting of the buttocks and extremities. The right anterior chest was prominent, and the fingers and toes were clubbed. The chest was emphysematous and hyperresonant, with diffuse, dry rales throughout. The abdomen was round, protuberant and tympanitic with active peristalsis. The liver and spleen were questionably enlarged. A white, glistening mass obstructed the right nares. The weight was 26.7 kg., and the height, 153 cm.

The temperature was 101°F., the pulse 110, and the respirations 20. The blood pressure was 90 systolic, 60 diastolic.

The urine was normal; the stools were light, foul smelling and fatty. The fat percentage of dry weight was 21.4. The stool nitrogen was 5.2 gm. in twenty-four hours. The white-cell count was 23,600, with 68 per cent neutrophils, 28 per cent lymphocytes and 4 per cent monocytes. The hemoglobin was 12.2 gm. The reticulocyte count was 0.8 per cent. The fasting blood sugar was 67 mg. per 100 cc. The total protein was 6.9 gm. per 100 cc. The prothrombin time was normal; the cephalin flocculation test was +++ in twenty-four and forty-eight hours. The bromsulfalein test was normal. The vitamin A tolerance test showed a fasting level of 0.1 units per cubic centimeter (carotenoids) and 0.1 units per cubic centimeter (vitamin A). Five hours after a test dose of oil-soluble vitamin A the levels were 0.1 and 0.6 units per cubic centimeter. The calcium was 8.3 mg. per 100 cc., and the phosphorus 3.6 and the alkaline phosphatase 8.6 units.

X-ray study of the chest demonstrated increased lateral and anteroposterior chest diameters and a low diaphragm (Fig. 1). Throughout both lungs there was irregular, strand-like, parenchymal density (Fig. 2). Clouding of all the nasal sinuses was found. The bones of the lumbar spine, pelvis, hands and wrists showed moderate generalized decalcification. The bone age was not retarded. Throat cultures demonstrated a varied flora on consecutive examination: Friedländer's bacillus,

Staphylococcus aureus and beta-hemolytic streptococcus. Two duodenal aspirations showed no tryptic enzyme activity.

The temperature and cough subsided on sulfadiazine and aerosol penicillin. The appetite was good. She was discharged after one month of hospitalization.

Second admission (four months later). During the first month after discharge sulfadiazine was continued at home, and the patient felt well. Following its discontinuance her condition was stabilized for a few weeks, but gradually recurrent cough, fever, weight loss and large, foul, frothy stools, averaging three or four each day, appeared. The physical signs were similar to those on the previous admission. On aerosol penicillin and streptomycin the symptoms subsided, and she was discharged one month after admission.

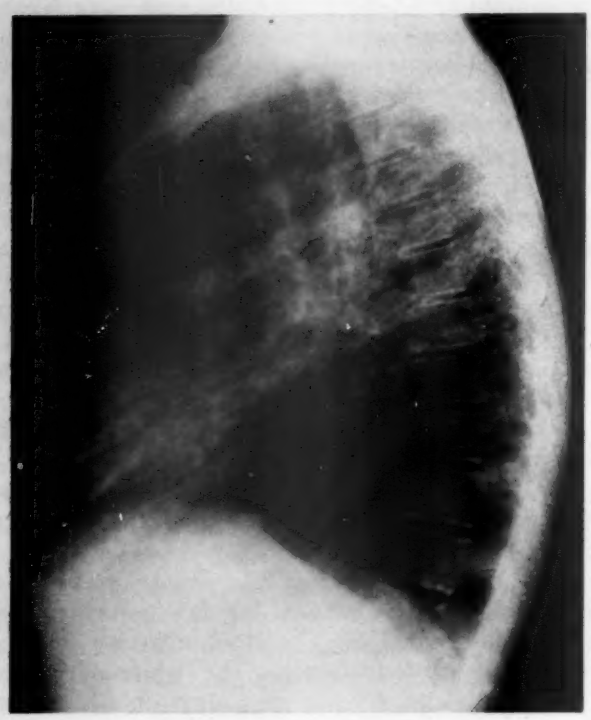

FIGURE 1.

Third admission (three months later). Complaints and findings were similar to those on the second admission. There was some improvement on aerosol penicillin. She was discharged two weeks after admission.

Final admission (one month later). For a few days preceding admission she became febrile, chilly, cyanotic, dyspneic and orthopneic, and she had paroxsyms of productive cough. On examination she was cyanotic. There was a small area of dullness and diminished breath sounds in the right base. The chest was otherwise hyperresonant. The liver edge was palpable two fingerbreadths below the costal margin. The temperature was 101.2°F., the pulse 120, and the respirations 28. The blood pressure was 100 systolic, 70 diastolic. An electrocardiogram was within normal limits. Sputum culture demonstrated abundant *Bacillus pyocyaneus* (*Pseudomonas aeruginosa*). She was digitalized and received oxygen, sulfadiazine and penicillin.

Five days after admission, following progressively labored dyspnea, increasing cyanosis and occasional disorientation, she died.

Differential Diagnosis

DR. RALPH A. ROSS: This story has all the stark, grim inevitability of a Greek tragedy. The patient had a family history of two siblings who died in infancy, one of chronic infection and the other of neonatal intestinal obstruction. The patient herself had a history of a large appetite throughout life, even in the midst of acute illness, bulky stools, with severe respiratory infection from childhood and with cough and nasal polyps since ten years of age. Physical examination disclosed malnutrition, a protuberant abdomen and emphysema, with clubbing, in addition to x-ray findings, which were apparently those of general pulmonary involvement leading to a sum total of what we call cystic fibrosis of the pancreas.

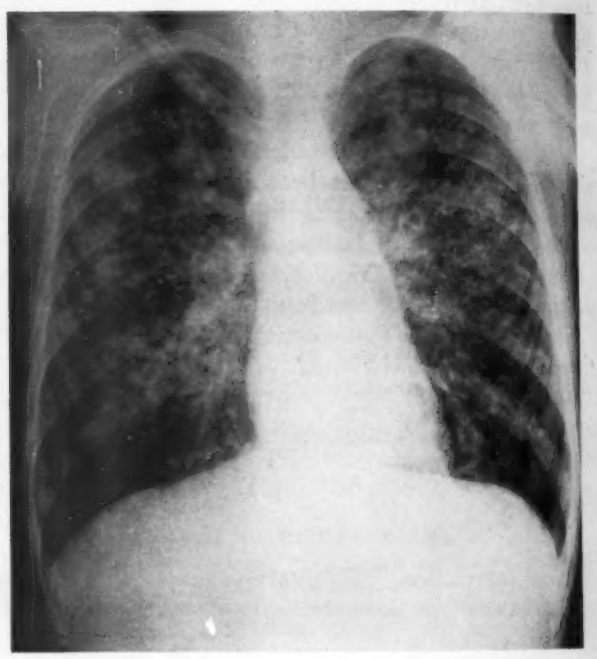

FIGURE 2.

May we see the x-ray films?

DR. JAMES J. MCCORT: An examination of the chest made on admission shows a patchy and mottled increase in density throughout both lung fields. Within this there are numerous radiolucent areas. The diaphragm is flat, and there is an

increase in the anteroposterior diameter of the chest. There is no detectable enlargement of the heart, and no fluid is present in the costophrenic sinuses.

Examination of the chest made five months after admission shows a slight increase in the pulmonary involvement particularly in the apical segments.

The final examination of the chest made nine months after the first admission discloses a definite progression of the pulmonary changes. The focal areas of increased density are more marked. There is more emphysema, as shown by further flattening of the diaphragm. An additional finding at this time is a slight prominence of the right ventricle as seen on the lateral film.

The films of the paranasal sinuses are of considerable interest. They show almost complete obstruction of the nasal fossa by a polypoid soft-tissue mass. Marked thickening of the mucous membrane, with polypoid change, is seen in the maxillary, ethmoid and sphenoid sinuses. The frontal sinuses remain clear.

DR. ROSS: Do you think there is alveolar involvement in the final film?

DR. MCCORT: There are irregular patches of density in the peripheral lung. We cannot be certain whether they are atelectatic lobules or cellular infiltration of the alveoli.

DR. ROSS: In arriving at this inevitable diagnosis we get help from the family history of one infant with chronic pulmonary disease, lasting eight months and ending in death; presumably, the same disease. An eight-week-old infant dying after persistent vomiting suggests, again without proof, that one child died of meconium ileus, a condition that has been described in association with cystic fibrosis of the pancreas in the newborn period. We know that the condition is commonly a familial, congenital disease. The persistent symptoms from early childhood — the voracious appetite, with rapid growth and apparent obesity — mean, I think, that this child met the requirement for growth by eating tremendous quantities, more than the average person, although a good deal was not absorbed as evidenced by the bulky, foul stools. The final occurrence of severe, persistent respiratory disease fills out the picture. The laboratory data of low serum calcium, the osteoporosis and the low vitamin A and carotenoids all indicate poor fat absorption. The absent tryptic enzyme activity shows that there was no pancreatic juice passing into the duodenum. The enlargement of the liver, with the suggestively positive cephalin flocculation test, also suggests the possibility of some cirrhotic changes in the liver, which have been described in pancreatic fibrosis. However, the final enlargement of the liver on the last admission suggests more to me right-sided heart failure due to prolonged pulmonary emphysema.

Pancreatic fibrosis in a thirteen-year-old child is unusual. Most of the cases previously presented in these gatherings have been in young infants or in children just above the age of infancy. There have been cases reported sporadically in the literature of older children — none older than fourteen and a half years. The striking situation here is the late onset of the alarming symptoms — the alarming symptoms being due not to nutritional deficiency but to infection of the respiratory tract.

The best that could be done with chemotherapy was to control the infection. The underlying disease of the mucous membranes indicated by polyps and progressive emphysema, with probable fibrosis in the lungs, was not controlled — the use of various chemotherapeutic agents caused the change from one pathogen to another, without finally being able to keep ahead of the disease. My diagnosis is, therefore, pancreatic fibrosis. Dr. Reyersbach may have some comments about our present experience with this disease.

DR. GERTRUD C. REYERSBACH: We have followed a number of children with this disease. The oldest we have is twelve and a half years old, having had diarrhea since birth and respiratory symptoms for five years. The next is ten years old and has had bulky stools since birth, respiratory symptoms starting at four years. Both these children have been treated with penicillin, streptomycin, and one also with a diet and pancreatin. We wonder whether we have helped these children to survive by therapy. When we go back to the literature we find quite a number of cases exactly the same as this in which the patients survived without therapy. Thus, the question whether our therapy helps is doubtful.

Our experience with treating the respiratory infection, which seems to be the lethal factor, has been disappointing. We are able to treat the *Staph. aureus*, the causative agent of the infection, generally found at first and quite successfully for a time. Then the staphylococcus is replaced by gram-negative organisms, *B. pyocyaneus*, colon bacillus and so forth. We add streptomycin in the

course of the disease. Often, all the organisms become drug resistant. We may have given this child help in combating the infection and may have prolonged life, but we have not made any definite changes.

Dr. Tracy B. Mallory: The experience is almost exactly similar to that of treating bronchiectasis with chemotherapeutic agents. One can change the bacterial flora very readily. One gets rid of the staphylococcus only to have it replaced with the colon bacillus. Whether the agents serve any useful purpose is very doubtful.

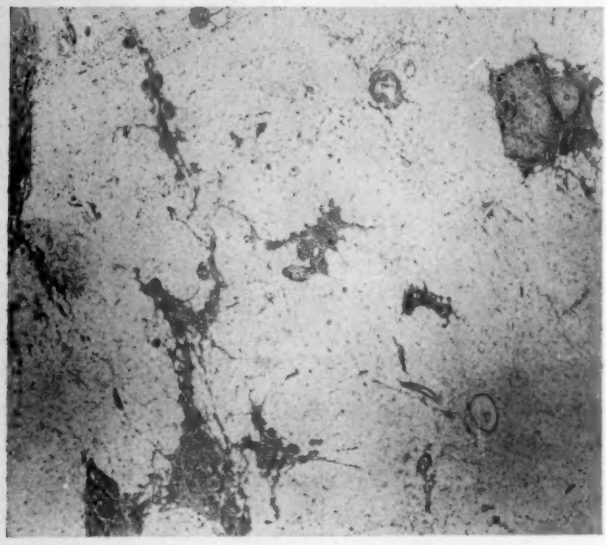

Figure 3.

Dr. Allan M. Butler: Your mention of bronchiectasis brings up the connection between a patient such as this and the group of cases Dr. Churchill's service has been interested in, characterized by nasal polyps, underdevelopment of the sinuses, chronic sinusitis, bronchiectasis and status inversus. What is the difference in the bronchiectasis of this group, who have no pancreatic fibrosis, as far as I know, and of patients with pancreatic fibrosis?

I do not know whether you found cirrhosis of the liver at post-mortem examination of this patient, but our findings on the ward made it suspect. It reminds one of the experience of Dr. Best with depancreatized dogs developing cirrhosis of the liver. Such cirrhosis could be prevented by the administration of choline or methionine. It is odd that in many patients who have no external secretions of the pancreas so little cirrhosis of the liver is indicated clinically. Dr. Best's work suggests that there is specific dietary therapy that might prevent this particular sequela.

Clinical Diagnosis

Pancreatic fibrosis.

Dr. Ross's Diagnoses

Fibrosis of pancreas.
Chronic pulmonary infection.
Cor pulmonale?
Cirrhosis of liver?

Anatomical Diagnoses

Atrophy of acinar tissue of pancreas, complete.
Bronchitis, chronic.
Emphysema.
Fat infiltration of liver, severe.
Biliary cirrhosis of liver.

Pathological Discussion

Dr. Mallory: We found very severe pancreatic disease, but there were no cysts and not a great deal of fibrosis. There was a small, fibrous area close to the head of the pancreas in about the spot where the pancreatic duct should have been, but we were entirely unable to identify the pancreatic duct. The remainder of the pancreas consisted of fatty tissue (Fig. 3) and islands of Langerhans that looked normal. There were no acinar cells left, so that the microscopical appearance was essentially what one sees following ligation of the main pancreatic duct and did not resemble the

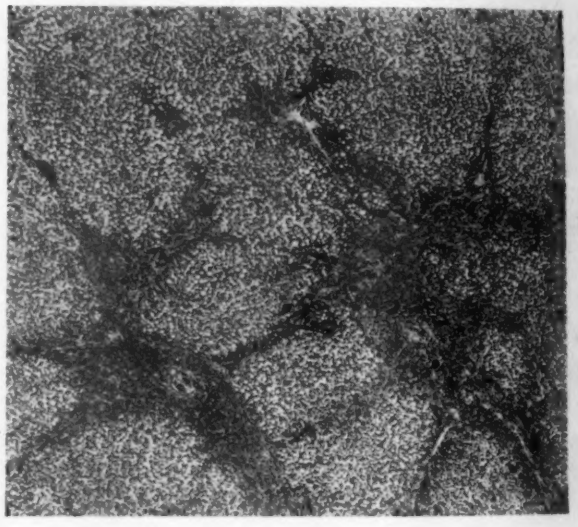

Figure 4.

usual picture of cystic fibrosis of the pancreas seen in infancy. Whether it is possible for the latter to develop to the stage of complete disappearance of acinar tissue, I have not the experience to say. Dr. Sidney Farber informs me that he does believe it is possible.

The lungs showed the characteristic picture that we see in cystic fibrosis. They were very large; the entire bronchial tree was filled with rather inspissated, purulent secretion. There was emphysema beyond the obstructed bronchi, and the infection had extended here and there into the alveolar lumens, but the great majority was still in the bronchi.

The organ that interested me most was the liver. This was greatly enlarged, weighing 2000 gm., which would be large for the liver of an adult, and was extremely large for this child. It was very fatty (Fig. 4), as one would expect to find the liver of an animal that had a total pancreatectomy and had been kept alive with insulin — the type that Chaikoff[1] and Best[2] and various others have described. There was cirrhosis but not a portal cirrhosis, which develops from the lack of pancreatic secretions, but a very clear-cut, biliary cirrhosis. All the small bile ducts were filled with plugs of inspissated material tinged with bile, although not consisting primarily of bile pigment (Fig. 5). I feel quite sure that the actual cirrhotic process was due to plugging of the bile ducts and was biliary in type. The fat infiltration, in contrast, might be traced to deficiency of pancreatic external secretion and had nothing to do with the development of the cirrhosis.

Dr. Butler: In Best's experimental animals he got fatty livers first, and then the cirrhosis seemed to come and replace the fatty liver, so that at one stage there was fatty liver and at a later stage cirrhosis.

Dr. Ross: Has this been seen in infants?

Dr. Reyersbach: Yes, it has. It is of interest because the clinical pictures vary so much in infants and in children in the same family — three siblings with the same disease — one dies at six months, the next one at six years, and the next at ten, twelve or fourteen years. Going through the autopsy reports and the literature, I happened to find that the condition described today has been found at least four times in infants as well as in children aged four or more.[3] Whether that is different from the usual fibrosis of the pancreas, I do not know.

Dr. Mallory: In the case reported by Siwe[4] the pancreatic lesion was apparently entirely similar to that in this case — complete replacement of

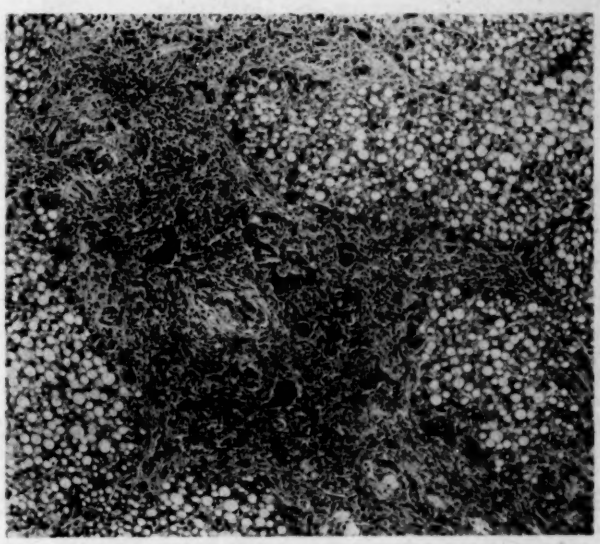

Figure 5.

acinar cells with adipose tissue and persistence of the islands of Langerhans. He interpreted it as agenesis of the acinar tissue. His case also showed cirrhosis of the liver, but as far as I can judge from his illustrations and description, it was portal rather than biliary in type.

References

1. Chaikoff, I. L., Connor, C. L., and Biskind, G. R. Fatty infiltration and cirrhosis of liver in depancreatized dogs maintained with insulin. *Am. J. Path.* **14**:101-110, 1938.
2. Best, C. H., Channon, H. J. and Ridout, J. H. Choline and dietary production of fatty livers. *J. Physiol.* **81**:409-421, 1934.
3. Andersen, D. H. Cystic fibrosis of pancreas and its relation to celiac disease: clinical and pathologic study. *Am. J. Dis. Child.* **56**:344-399, 1938.
4. Siwe, S. A. Über die exokrine Funktion des Pankreas und die Folgen ihres Wegfalles: ein Fall von fast totaler Agenesie des exokrinen Teiles des Pankreas. *Deutsches Arch. f. klin. Med.* **173**:339-358, 1932.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society
Owned by the Massachusetts Medical Society and
Published Weekly under the Jurisdiction of the
Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. John Fallon, M.D.

Joseph Garland, M.D., Editor

Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Clara D. Davies, Executive Editor
Robert O'Leary, Assistant Editor

Editorial Board
C. Guy Lane, M.D. Maxwell Finland, M.D.
Henry R. Viets, M.D. James M. Faulkner, M.D.
Robert M. Green, M.D. Carroll B. Larson, M.D.
Dwight O'Hara, M.D. Francis D. Moore, M.D.
Fletcher H. Colby, M.D. C. Stuart Welch, M.D.
Robert L. Goodale, M.D. Vernon P. Williams, M.D.
Chester M. Jones, M.D. Benjamin Castleman, M.D.
Harvey R. Morrison, M.D. Hugh R. Leavell, M.D.

Subscription Terms: $7.00 per year in advance, postage paid, for the United States (medical students, $4.00 per year); Canada, $8.00 per year (Boston funds); $9.50 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, three weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications, *including those concerning classified advertising but not those regarding other advertising*, should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

New England Advertising Representative (*except for classified advertising*): Edwin B. Tyler, 89 State Street, Boston, Massachusetts. Telephone LA 3-5516.

ONE WORLD

The relations of human beings, one with another, too often represent the very extremes of human conduct. Bitterness and hate and cruelty as expressed by individuals and nations and races is thrown into sharp contrast with those great emotional surges of tenderness and compassion that at other times may animate almost all men and seem at all times to animate some of them.

The consciences and the emotions of the common people of a nation tend in the main to direct their thoughts and activities into the channels of compassion. Thus the people of this country, coldly as they may sometimes have been viewed by their fellow citizens of a world drawn closer together by mutual interdependence and swift travel, still pride themselves on their generosity and their feeling of good will toward the common people of all other nations.

Aside from the vast gifts that national policy has dictated should be put into the hands of the Wise Men for distribution to our stricken neighbors, there has been a constant flow of more spontaneous, if lesser, offerings of good will to all those who suffer and who could be reached.

The air bridge to Berlin has carried more than food for the mouths and coal for the bins of our recent enemies and present wards; it has carried good will in a franker form to the children of that city under siege as a spontaneous expression of kindliness and generosity on the part of American airmen.

Santa Claus in numerous guises and directing a variety of carriers, working in all seasons and without vacation, has delivered a continuous stream of freely offered gifts from these shores to all available quarters of the globe. And yet these earnests of good intention on the part of a people conscious of its own favorable situation represent but one manifestation of a general good feeling that needs only the opportunity to prevail. Various religious and sociologic organizations have this year held meetings on an international plane, not the least among them being the World Council of Churches, the World Health Organization and the World Medical Association. The United Nations stand ready to hang a Christmas wreath on the door of nearly every country in the world and even, with some trepidation, to pin one upon the Iron Curtain itself.

The United States, at long last, has officially admitted and sincerely welcomed a new band of pilgrims to set foot upon her shores — at the Thanksgiving season, with fitting symbolism. May their Christmas in a new land be a happy one, and may this land fulfill the promises of freedom and opportunity that it has so far seemed to these displaced persons to offer!

Each year at this time it is well to remember that good will is communicable; that if enough people wish it "Earth shall be fair and all her people one"; that through their will they may yet see peace on earth.

MASSACHUSETTS PHYSICIANS COMMITTEE

On November 22, 1948, a group of physicians from various parts of the Commonwealth met and voted to form a Massachusetts Physicians Committee for the purpose of promoting free enterprise and the preservation of a system of private practice in medicine in this country. This committee was formed not to oppose, but to assist; not to hinder but to help; not to destroy but to build up. Believing in the same health goal, if not in the methods of reaching it, that Mr. Ewing has established in his report to the President — namely, the extension of the best possible medical services to all the people of the country, — it offers its assistance in helping to achieve those ends by the best possible means.

It believes that this goal can be most nearly approximated by preserving the system of private medical practice with all the reforms and safeguards for the people that experience may suggest, by the promotion and extension of voluntary prepayment plans, and by assisting government at the most effective level in furnishing the same adequate service to those who cannot afford to bear their share of the costs.

This committee is fearful of the waste and extravagance and inefficiency that may accompany an attempt at reaching the common goal by means of any system of compulsory, tax-supported or political medicine. It is fearful of the distance that such a system, however innocuous it appears at the beginning, may eventually travel.

It does not believe, as the chairman of the Committee for the Nation's Health believes, "that national health insurance does not mean regimentation of doctors or state control, and will not interfere in any way with the doctor-patient relationship." It does agree with him that "The time has come to take the politics out of health," but it does not agree that the passage of a bill for government-controlled national health insurance will achieve that end.

Working in harmony with the organized profession of medicine and with all other healthy interests, it invites the help of the physicians of the Commonwealth in studying these matters of general concern, in enlightening the public and in lending all the aid possible to the Government and the people in establishing the health care of the nation on a secure basis.

UNDERGRADUATE INSTRUCTION IN ALLERGY

A comprehensive survey has clearly demonstrated that satisfactory instruction in allergy is not being provided in the majority of the leading medical schools today. New England institutions, unhappily, prove no exception to the rule. This conclusion is based upon the results of a questionnaire[1] returned by sixty-six schools, less than half of which were found to have an acceptable minimal curriculum in allergy.

Should such an observation call forth the comment "why bother our students about sneezes, wheezes and itches," the answer seems clear. Few can deny that many young internists have completed their medical training with little or no contact with allergy or allergic thought.[2] Some medical and much lay opinion still classes allergy as a narrow specialty whose chief qualification is the ability to perform and the inability to interpret skin tests. On the contrary, altered reaction in general is the province of the allergist. Such a heading embraces the principles of sensitivity, of anaphylaxis, of immunology. It includes altered reactivity to proteins, bacteria, nonbacterial substances and drugs. Allergy is concerned with the practical management and pathogenesis of many diseases. It is closely interrelated with the fields of bacteriology, biochemistry, pathology, metabolism, circulatory disorders and psychosomatic medicine — in short, it is part and parcel of internal medicine.

No allergist can fulfill his maximum responsibility to his patients and to his specialty unless he has a background of sound medical training. In like manner, no internist should be regarded as well trained in internal medicine unless he is thoroughly

cognizant of the principles of anaphylaxis and allergy and of their application to medicine. It is high time that departments of medicine recognized the need of adequate undergraduate training in allergy. They should then take steps to obtain suitable facilities and to organize them in such a manner as to provide systematic and enlightened training.

REFERENCES

1. Swineford, O., Jr. Undergraduate education in allergy: report of Subcommittee on Undergraduate Education in Allergy of American Academy of Allergy. *J. A. Am. M. Coll.* **21**:265-270, 1946.
2. Barr, D. P. Relationship of allergy to medicine. *J. Allergy* **16**:61-68, 1945.

GUIDE TO HEALTH SERVICES

A USEFUL key to the health services available in the Greater Boston area has been prepared by the Boston Health League and sent to all physicians practicing in the area. Arranged according to type of specialized service, the information it offers runs the scale from adoption and care of the aged to well-baby conferences, workmen's compensation and x-ray services.

The complexity of the facilities available in a great metropolitan area make such a handbook nearly indispensable. With the *Handbook for Physicians* published by the Massachusetts Department of Public Health, and the *Directory of Social Service Resources of Greater Boston*, emanating from the Greater Boston Community Council, it completes an invaluable triad of such guides.

OBITUARY

ABRAHAM MYERSON (1881-1948)

The death of Dr. Abraham Myerson on September 3, 1948, in his sixty-seventh year ended a distinguished medical service of more than thirty-five years in this community.

Dr. Myerson graduated from Tufts College Medical School in 1908. After a period of practice in Boston he trained for a career in neuropsychiatry by serving as resident neurologist to Alexian Brothers Hospital in St. Louis, 1912-1913, and assistant physician to the Boston Psychopathic Hospital, 1913-1914. From 1914 to 1918 he was pathologist and clinical director of the Taunton State Hospital; from 1918 to 1920 he served as chief medical officer of the outpatient department of the Boston Psychopathic Hospital. Thus he acquired a background and experience in neurology, neuropathology and intramural and extramural psychiatry. His teaching experiences began in St. Louis and were continued in Boston. He became professor of neurology at Tufts College Medical School and taught this subject in an inspiring manner to generations of medical students. He was clinical professor of psychiatry at Harvard Medical School. Throughout his life his interests encompassed both neurology and psychiatry. He was visiting neurologist to the Boston City Hospital, neuropsychiatrist to the Beth Israel Hospital and consultant in neurology or psychiatry to several other institutions.

Dr. Myerson became interested in research early in his medical career, and for more than thirty-five years he made outstanding contributions to medical literature. Two of his early interests were syphilis of the nervous system and genetics, and to the end he continued to investigate and report on these subjects. The scope of his research interests widened greatly, encompassing the effects of social, environmental and internal stresses on the one hand and metabolic and biochemical changes concomitant to mental illness on the other. The first group of studies are found in books from his pen, namely, *The Nervous Housewife*, *Foundations of Personality* and *When Life Loses Its Zest*. Many papers appearing in the medical literature document other types of work. In recognition of his abilities and accomplishments a research building was erected at the Boston State Hospital, and, aided by a large grant from The Rockefeller Foundation, he became director of research of an active organization.

He was a member of many medical societies, served on many committees and was elected president of several. He published eight books and more than a hundred and fifty scientific papers.

These cold facts give no adequate picture of Abraham Myerson. His dynamic personality, his speaking ability, his quick wit and humor, his logical thinking, his friendliness and his devotion to social improvement, civic affairs and human rights are more to the point. He was a stimulating teacher, guide and friend to students. He was a leader of many younger colleagues in their research efforts. He was a most popular lecturer to lay groups and was ever ready to interpret psychiatry to the laity as well as to his medical colleagues.

He was strong in his opinions and fearless in his expression of them. Book reviews by Myerson were forthright, explicit and critical. Praise was not withheld when considered merited, but statements inimical to his point of view were brilliantly and vigorously attacked. He was a strong and articulate opponent of psychoanalysis. To do justice to the subject and express his opinion, he read everything written by Freud as well as a vast amount of other psychoanalytic literature, becom-

ing almost encyclopedic in his knowledge of literature on this subject.

With great dynamic qualities of personality, with deep erudition and learning, with brilliance, wit and articulateness, with strong emotional devotion to good causes and with a great store of energy he was indeed a force in the medical world — local, national and international. Perhaps no better testimony of his influence is needed than the fact that his two sons follow his footsteps in neuropsychiatry and his daughter is training in psychiatric social work.

A final word about his strength of character and great spirit is due. For seven years he was aware that he had a progressive cardiac ailment. Never for an instant did he seek sympathy; never did his broad interest in science and literature diminish. Until his last hours he continued his intellectual efforts and only wondered how much he could accomplish in the brief interval before death would stop him.

H. C. S.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

Barton — Robert B. Barton, M.D., of Wellesley Hills, died on November 30. He was in his forty-eighth year.

Dr. Barton received his degree from Boston University School of Medicine in 1926. He was a fellow of the American Medical Association.

His widow and two daughters survive.

Paine — N. Emmons Paine, M.D., of Walpole, died on November 30. He was in his ninety-sixth year.

Dr. Paine received his degree from Albany Medical College in 1875. He was the founder of the Newton Sanatorium and was formerly superintendent of the Westboro State Hospital and a member of the staffs of Newton-Wellesley Hospital and Massachusetts Memorial Hospitals. He was professor emeritus of psychiatry at Boston University School of Medicine and was a fellow of the American College of Physicians and the American Psychiatric Association.

A son and two daughters survive.

Schwager — Solomon Schwager, M.D., of Pittsfield, died on November 30. He was in his fifty-eighth year.

Dr. Schwager received his degree from New York University College of Medicine in 1917. He was a fellow of the American Medical Association.

His widow and two sons survive.

CORRESPONDENCE

DOCTOR DRAFT

To the Editor: The editorial entitled "Concerning the Doctor Draft," which appeared in the November 11 issue of the *Journal*, contains the following statements:

> . . . Congress's contemplated action will concern chiefly doctors who were trained under ASTP and V–12 at Government expense but were unable to complete their term of active duty. . . . If they should be required to complete their contract by a few months of peace-time service, it would seem too reasonable a sacrifice to be fairly resented.

There are a few errors here.

In the first place, we completed our term of active duty as determined by the Army and Navy.

Secondly, we have no contract broken or otherwise with the Government. With the exception of those who volunteered for the inactive reserve, we all have certificates of honorable discharge — no strings attached.

Finally, most of my colleagues who are former ASTP'S or V–12's do not resent being drafted if it is necessary. We do resent slander and lies concerning us, especially in the press.

Are you brave enough to print this in toto?

Kenneth Bruns
Senior Medical Student
Formerly AS V–12 USNR

4933 Forest Park
St. Louis, Missouri

Note: In a literal sense Mr. Bruns is exactly right, although careful examination fails to reveal any hint of disparagement or slander in the wording of the editorial. Certainly none was intended. "Contract" was broadly used in the sense of implied obligation to repay the Government's investment by a period of active duty. ASTP's and V–12's who have served the originally intended term of active duty are morally quits with the Government that paid their tuition; those who have not (through no fault of their own, as specified in the editorial) have certainly broken no contract. However, many of them, and apparently Mr. Bruns among them, are still conscious enough of an obligation to be willing to discharge it in full when and if the necessity arises. In this they show themselves to be patriotic, responsible and fair-minded citizens, differing in no way from the overwhelming majority of the medical profession. — Ed.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Headache and Other Head Pain. By Harold G. Wolff, M.D., professor of medicine (neurology) and associate professor of psychiatry, Cornell University Medical College, and attending physician, New York Hospital, New York. 8°, cloth, 642 pp., with 154 illustrations. New York: Oxford University Press, 1948. $12.00. (Oxford Medical Publications.)

The author in this comprehensive book summarizes his studies of fifteen years on the subject of head pain, including migraine in all its aspects and relations. Selected bibliographies are appended to the various chapters. The publishing is well done. The book is recommended for all medical libraries and should prove valuable to all neurologists and other physicians interested in the subject.

Voluntary Medical Care Insurance in the United States. By Franz Goldmann, M.D. 8°, cloth, 228 pp. New York: Columbia University Press, 1948. $3.50.

This book, a companion to *Public Medical Care*, describes and analyzes the development and present state of voluntary medical care insurance and appraises the most important types of organizations in the United States, including profit, nonprofit and group plans. The volume is well published and should be in all medical, public and insurance libraries.

NOTICES

ANNOUNCEMENTS

Dr. Harold I. Miller announces the opening of an office for the practice of general surgery at 311 Commonwealth Avenue, Boston.

Dr. Edward S. Stone announces the removal of his office from 276 to 314 Commonwealth Avenue, Boston, near Massachusetts Station, for the practice of ophthalmology.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in Building E, Harvard Medical School, on Tuesday, December 21, at 8:15 p.m. A symposium on virus diseases will be presented, with Dr. John F. Enders as chairman.

PROGRAM

The Diagnosis of Virus Diseases of the Respiratory Tract. Dr. Maxwell Finland.

The Prevention and Treatment of Virus Diseases of the Respiratory Tract. Dr. Monroe D. Eaton.

Recent Advances in the Diagnosis and Treatment of Certain Rickettsial Diseases. Dr. John C. Snyder.

The Interpretation of Reactions Following Smallpox Vaccination. Major Abram S. Benenson, M.D.

AMERICAN ASSOCIATION OF SCHOOLS OF SOCIAL WORK

The American Association of Schools of Social Work will hold its thirtieth annual meeting at the Hotel Statler, Boston, on January 27, 28 and 29, 1949.

MAINE MARITIME ACADEMY

A position of medical officer is available for the annual cruise of the Maine Maritime Academy, which begins on January 8 and continues until April 4, 1949. A straight fee of $1000, in addition to maintenance for the three months' cruise, is usually paid.

Further information regarding qualifications may be obtained from the Superintendent, Maine Maritime Academy, Castine, Maine.

NATIONAL FOUNDATION FOR INFANTILE PARALYSIS FELLOWSHIPS

The National Foundation for Infantile Paralysis announces that the following fellowships are available to qualified applicants: research fellowships in virology, orthopedic surgery, pediatrics, epidemiology and neurology (available to doctors of medicine, or, when appropriate, doctors of philosophy, the former having a minimum of two years of training on the residency level, of sound health, as attested by a physical examination, citizens of the United States who can present an appropriate program of study and investigation); clinical fellowships in physical medicine for physicians who wish to prepare for eligibility for certification by the American Board of Physical Medicine (available to graduates of Class A medical schools who have completed a rotating internship of not less than one year in a hospital approved by the Council on Medical Education and Hospitals of the American Medical Association, licensed to practice medicine in one or more states, citizens of the United States, forty years of age or younger and of sound health, as attested by a physical examination); and fellowships in public health for postgraduate study leading to the degree of Master of Public Health at a school of public health approved by the American Public Health Association (available to graduates of Class A medical schools who have completed not less than one year of internship in a hospital approved by the Council on Medical Education and Hospitals of the American Medical Association, licensed to practice medicine in one or more states, citizens of the United States and of sound health as attested by a physical examination).

For further information regarding the fellowships, application should be made to the National Foundation for Infantile Paralysis, 120 Broadway, New York 5, New York. Selection will be made on a competitive basis by committees composed of specialists in each field, and awards will be based on the individual needs of the applicants.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, February 4, 1949.

Arrangements will be made so far as possible for candidates to take the Part I examination (written paper and submission of case records) at places convenient for them. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held May 8 to 14 inclusive, 1949, at the Hotel Shoreland, Chicago, Illinois. Notice of the exact time and place of the Part I and Part II examinations will be sent all candidates well in advance of the examination date.

New bulletins are now available for distribution upon application and give details of all changes in Board requirements and regulations made at the annual meeting of the Board held in Washington, D. C., May 16 to May 22, 1948. These apply both to candidates and to hospitals conducting residency services for training.

Application forms and bulletins will be sent upon request made to the American Board of Obstetrics and Gynecology, Inc., 1015 Highland Building, Pittsburgh 6, Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 23

FRIDAY, DECEMBER 24

*9:00–10:00 a.m. Craniopharyngioma, Ophthalmic Type, due to Pituitary Tumors (Demonstration and Discussion of Cases Operated on by Transsphenoidal Methods). Dr. Oscar Hirsch. Joseph H. Pratt Diagnostic Hospital.

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

MONDAY, DECEMBER 27

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

5:15 p.m. Staff Meeting. Harris Hall, New England Deaconess Hospital.

TUESDAY, DECEMBER 28

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, DECEMBER 29

*11:00 a.m.–12:00 m. Medical Rounds. Amphitheater, Children's Hospital.

*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Hospital). Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

OCTOBER 1–MAY 20. Metropolitan State Hospital. Page 418, issue of September 9.

NOVEMBER 17–JANUARY 26. Boston State Hospital Psychiatric Seminar Schedule. Page 762, issue of November 11.

DECEMBER 21. South End Medical Club. Page xiii, issue of January 9.

DECEMBER 21. Greater Boston Medical Society. Notice above.

JANUARY 13, 1949. The Present Status of the Peptic Ulcer Problem. Dr. S. Allan Wilkinson. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

JANUARY 27–29, 1949. American Association of Schools of Social Work. Notice above.

MARCH 7–9, 1949. American Academy of General Practice. Page 728, issue of November 4.

MARCH 28–APRIL 1, 1949. American College of Physicians. Page 158, issue of July 22.

MAY 16–19, 1949. American Urological Association. Biltmore Hotel, Los Angeles, California.

MAY 24–26, 1949. Massachusetts Medical Society. Annual Meeting Worcester Municipal Auditorium, Worcester.

MAY 26–28, 1949. American Goiter Association. Hotel Loraine, Madison, Wisconsin.

MAY 30–JUNE 3, 1949. International Congress on Rheumatic Diseases. Page 800, issue of November 18.

NOVEMBER 11–17, 1949. Third Inter-American Congress of Radiology. Page 158, issue of July 22.

DISTRICT MEDICAL SOCIETIES

HAMPDEN

JANUARY 25. 8:30 p.m. Academy of Medicine, Springfield. A Review of the Sterility Problem. Dr. John Rock.

MIDDLESEX EAST

JANUARY 19.
MARCH 23.
MAY 11.

WORCESTER NORTH

FEBRUARY 23. Burbank Hospital, Fitchburg.
APRIL 27. Annual Meeting.